Archives of Dermatology and Syphilology

VOLUME 27 JUNE, 1933 NUMBER 6

PULMONARY EMBOLISM FROM ARSENICALS INJECTED INTRAVENOUSLY

A METHOD SUGGESTED FOR PREVENTION

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Fortunately, severe and undesirable reactions from the intravenous administration of drugs are not frequent; but this fact should not permit one to overlook the dangerous and fatal results which can occur.

Fatalities from arsphenamine have been observed ever since Ehrlich first introduced the drug, and much work has been done on the problem, but a great majority of the work has been concerned with the "nitritoid crises," and rightly so, since they constitute the cause of most of the deaths from arsphenamine. However, in this report I shall limit the discussion to the production of pulmonary embolism by this form of treatment.

My interest was aroused by an autopsy which was performed on a young man who died from multiple abscesses of the lungs due to pulmonary embolism caused by an injection of neoarsphenamine, and this work was undertaken in order to investigate the mechanism of the production of pulmonary embolism by the intravenous administration of arsenical drugs.

INCIDENCE

Since the World War, the parenteral administration of drugs has rapidly come to the fore, and at the present time almost any drug can be secured in ampules suitable for this type of therapy.

Coincident with the increase in the use of this form of treatment, there has occurred a marked rise in the incidence of pulmonary embolism, which some authors, for instance Kuhn,[1] attribute largely to the intravenous method of administration.

From the Department of Pathology of the University of Colorado School of Medicine, under the direction of Dr. William C. Johnson, Professor of Pathology.

1. Kuhn, J. K.: Die Bewegung der Thrombosen und Embolien in den Nachkriegsjahren und ihre Ursachen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **41**:329, 1929.

Reactions occurring during the treatment of syphilitic patients have led to the publication of a large number of articles on the subject and also to the compiling of statistics relative to the number of treatments and the number of deaths.

The Cologne Commission [3] reported the aggregate death rate from arsphenamine to be 1 death in 11,289 injections, while Stokes [4] personally observed 9 deaths in 63,000 injections, or a ratio of 1:7,000.

Reports from the medical department of the United States Navy [5] show that during the years from 1925 to 1928 its members administered 273,354 intravenous injections of arsenicals. During this period, there were 16 deaths from neoarsphenamine and 1 death from arsphenamine, or an average ratio of 1 death for every 16,079 injections. Similar reports from the German Government [5] set the ratio at 1 death for every 10,984 injections, while the British Government stated that the ratio was 1 death for 13,000 injections.

The majority of these deaths were, no doubt, due to the so-called "nitritoid crisis," but a survey of the cases reported in the literature indicates that a goodly number were due to pulmonary embolism.

Statistics of the United States Public Health Service [6] show that at the present time about 643,000 people in this country are receiving treatment for syphilis. This must be a conservative figure in view of the fact that many cases are not reported. If each patient receives 25 injections annually (and this is a fair average, since so many patients receive the intensive form of treatment), the physicians of the United States administer each year approximately 16,075,000 intravenous injections of arsenicals.

Therefore, according to the ratio established by the statistics of the United States Navy, which is far lower than that in any other country, there must be annually in the United States about 852 deaths from arsenical drugs, a large proportion of which are due to pulmonary embolism.

On first thought, this number seems incredible, for one concludes that, were this the case, surely there would be more cases reported. But when one considers that the majority of these deaths occur at the

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2. Deleted by author.

3. Meirowsky: Die Ergebnisse der Kölner Salvarsanstatistik, Deutsche med. Wchnschr. **46**:299, 1920.

4. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926.

5. Phelps, J. R.: A Statistical Study of the Results of 272,354 Injected Doses of Neo-Arsphenamin and Other Compounds of Arsenic, U. S. Nav. M. Bull. **28**: 659, 1930.

6. Usilton, L. D.: Prevalence of Venereal Disease in United States, Ven. Dis. Inform. **11**:543, 1930.

hands of physicians many of whom know nothing of the serious results which may follow such therapy and do not in any way connect the death with the injection of the drug, it is easy to see that these figures may not be so incredible.

Raiziss [7] also is of the opinion that the estimates of fatalities following the intravenous injection of neoarsphenamine and arsphenamine are low, and that the number of deaths is larger, since many of the known fatalities do not appear in the statistics reported in the literature.

HISTORY

As far as could be determined, Michaelis,[8] in 1911, was the first to suggest that fatalities resulting from arsphenamine were due to the precipitates found in the blood after injections of the drug.

Von Miessner,[9] in the same year, performed autopsies on animals dying of hoof and mouth disease which had received injections of acid arsphenamine, and found multiple emboli and thrombi in the pulmonary arterioles. He also conducted experiments in vitro with acid and with alkaline solutions, and stated that both types of solution produced precipitates.

Joseph [10] corroborated the work of Miessner and demonstrated that acid arsphenamine, when injected intravenously, caused precipitates in the blood which resulted in emboli in the right ventricle of the heart and the pulmonary arterioles. However, no such action on the part of alkaline solutions was demonstrated.

McKee,[11] in 1912, also demonstrated the formation of precipitates in the blood by intravenous injections of acid arsphenamine.

The first real attempt at an explanation of the cause of this precipitate was advanced by Danysz [12] in 1917. He conceived the idea that arsphenamine was acted on by the carbon dioxide and sodium bicarbonate of the blood and changed to an insoluble base which remained in the circulation until removed by the leukocytes and the organic bases

7. Raiziss, G. W., and Koppelman, A.: Reactions Following the Administration of Arsphenamin and Its Derivatives, J. Chemotherapy **4**:7, 1927.

8. Michaelis, L.: Die Ehrlich-Hata Behandlung in der inneren Medizin, Deutsche med. Wchnschr. **36**:2278, 1910.

9. von Miessner, H.: Die Ursache für die giftige Wirkung saurer Salvarsanlosungen, Deutsche med. Wchnschr. **37**:491, 1911.

10. Joseph, D. R.: On the Formation of Precipitates After the Intravenous Injection of Salvarsan, J. Pharmacol. & Exper. Therap. **14**:83, 1919.

11. McKee, G. M.: A Study of the Blood After Intravenous Injections of Salvarsan, J. Cutan. Dis. **30**:199, 1912.

12. Danysz, J.: Les propriétés physico-chimiques des produits du groupe des arsénobenzènes; leurs transformations dans l'organisme, Ann. Inst. Pasteur **31**: 114, 1917.

of the plasma. He stated that the calcium, sodium and magnesium phosphates as well as the chloride salts of iron in the blood had a similar action on the drug. He concluded that the immediate reactions were due to emboli resulting from an increase in the calcium biphosphate and other electrolytes in the blood, and that the degree of toxicity of the drug depended on the degree of rapidity of its precipitation from solution.

Fleig [13] and Queyrat [14] demonstrated that acid solutions of arsphenamine would combine with plasma, in vitro, to form precipitates, and that they also hemolyzed erythrocytes. By injecting these solutions into rabbits, they found that precipitates resulting in embolism and death invariably resulted.

Jackson and Smith,[15] in an effort to confirm Danysz' theory in regard to the action of calcium phosphates and carbon dioxide, conducted experiments on dogs in which they injected large amounts of calcium salts with the arsphenamine or increased the carbon dioxide content of the blood prior to injection of the drug, but they were unsuccessful in producing embolism.

In line with the ideas expounded by Danysz, the precipitates were thought by Jacobsohn and Sklarz [16] to be due to a vegetable diet which resulted in an increase in the potassium and arsenic ions and a decrease in the calcium ions in the blood. They believed this to be the cause of the increased number of reactions in Germany just after the war.

On the other hand, Jeanselme and Pomaret [17] tried to show that the reactions were due to a high protein diet, which increased the acidity of the blood.

Berman [18] advanced the theory that there was a very high protein content of the blood in syphilitic patients, and that the precipitation was due to a combination of the drug and these proteins.

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13. Fleig, C.: La toxicité du salvarsan, Paris, A. Maloine, 1914.

14. Queyrat, M. L.: Salvarsan et néo-salvarsan; de quelques réactions du foie consecutives à leur injection; meiopragie hépatiques a type urobilinurique, Bull. et mém. Soc. méd. d. hôp. de Paris **38**:299, 1914.

15. Jackson, D. E., and Smith, M. I.: An Experimental Investigation of the Cause of Early Death from Arsphenamin and of Certain Other Features of the Pharmacological Action of the Substance, J. Pharmacol. & Exper. Therap. **12**:221, 1918.

16. Jacobsohn, F., and Sklarz, E.: Zur Pathogenese der Salvarsanschädigungen, Med. Klin. **18**:567, 1922.

17. Jeanselme, E., and Pomaret, M.: Recherches expérimentales sur le "choc" par les corps phenoliques, Ann. de méd. **10**:467, 1921.

18. Berman, L.: The Nitritoid Crisis After Arsphenamin Injection, Arch. Int. Med. **22**:217 (Aug.) 1918.

Schamberg,[19] conducting experiments similar to Berman's, was unable to find any increase in the protein content of the blood of syphilitic persons, and stated that the precipitate was composed of the drug alone, since he could dissolve it with sodium hydroxide. He was of the opinion that the occurrence of the precipitate was due to the variation in the amount of alkali in different lots of asphenamine.

The work of Oliver and Douglas[20] as well as of others has shown definitely that the precipitate consists of both the drug and protein and not of the drug alone as Schamberg believed.

Recently, efforts have been made to demonstrate that the precipitation is a result of colloidal changes in the blood. Klemensiewicz[21] and Raiziss and Gavron[22] have shown that neoarsphenamine and acid arsphenamine are strongly colloidal in action. Hirschfelder and Wright,[23] studying neoarsphenamine with the ultramicroscope, found that it exhibited the properties of a typical lyophilic colloid. Hunter and Patrick[24] have done some important work on the colloidal nature of the arsphenamines, as will be brought out later.

A review of the literature revealed forty-eight cases of accidents from intravenous therapy, and a summary will be given later. The case reported in detail is the one observed by me and the one responsible for this work.

REPORT OF A CASE

History.—A white man, aged 29, entered the hospital on Oct. 9, 1931, complaining of pain in the right side of the chest, cough and bloody sputum. On October 4, he began to feel exhausted on slight exertion. On October 6, a sharp, knifelike pain developed in the right side of the chest, which was more pronounced on deep inspiration. His condition grew worse, and he was sent to the hospital by a private physician. When admitted, he was dyspneic, cyanotic and in a critical state. Examination of the chest showed dulness in the right axillary space and over the base of the left lung. A friction rub was heard over the bases of both

19. Schamberg, J. F.; Tukuda, K., and Kolmer, J. A.: A Study of Arsphenamin Serum Precipitates and Their Relation to Clinical Reactions, Arch. Dermat. & Syph. **3**:263 (March) 1921.

20. Oliver, J., and Douglas, E.: Biological Reactions of Arsphenamin: Its Reaction with Plasma Proteins and Certain Hydrophilic Colloids and the Relation of These Processes to the Phenomena of Protection, Arch. Dermat. & Syph. **7**:778 (June) 1923.

21. Klemensiewicz, Z.: Sur les propriétés colloidales des solutions aqueuses du salvarsan, Bull. Soc. chim. de France **27**:820, 1920.

22. Raiziss, G. W., and Gavron, J. L.: A Study of the Colloidal Properties of Arsphenamin and Allied Products, J. Pharmacol. & Exper. Therap. **20**:163, 1922.

23. Hirschfelder, A. D., and Wright, H. N.: The Ultramicroscopic Examination of Neo-Arsphenamin and of Certain Antiseptics and Their Effects on Protein Solutions, J. Pharmacol. & Exper. Therap. **39**:13, 1930.

24. Hunter, A. S., and Patrick, W. A.: Studies on the Physical and Colloidal Chemistry of Arsphenamin, J. Lab. & Clin. Med. **10**:446, 1925.

lungs. Bronchial breathing and fine râles were heard over the axillary and basal regions. There was a leukocyte count of 19,000, with 93 per cent polymorphonuclears. There were albumin, blood and pus cells in the urine. A diagnosis of bilateral pneumonia was made. Roentgen examination showed a diffuse mottling of both lungs.

The patient was treated symptomatically, but gradually failed. The pulse became rapid and of poor quality. Cyanosis and dyspnea became marked, and the patient died in coma on October 14.

Autopsy.—The right lung was bound to the wall of the chest and to the diaphragm by fibrous adhesions anteriorly and laterally and by fibrinous adhesions posteriorly. The right pleural cavity contained about 100 cc. of bloody fluid. The

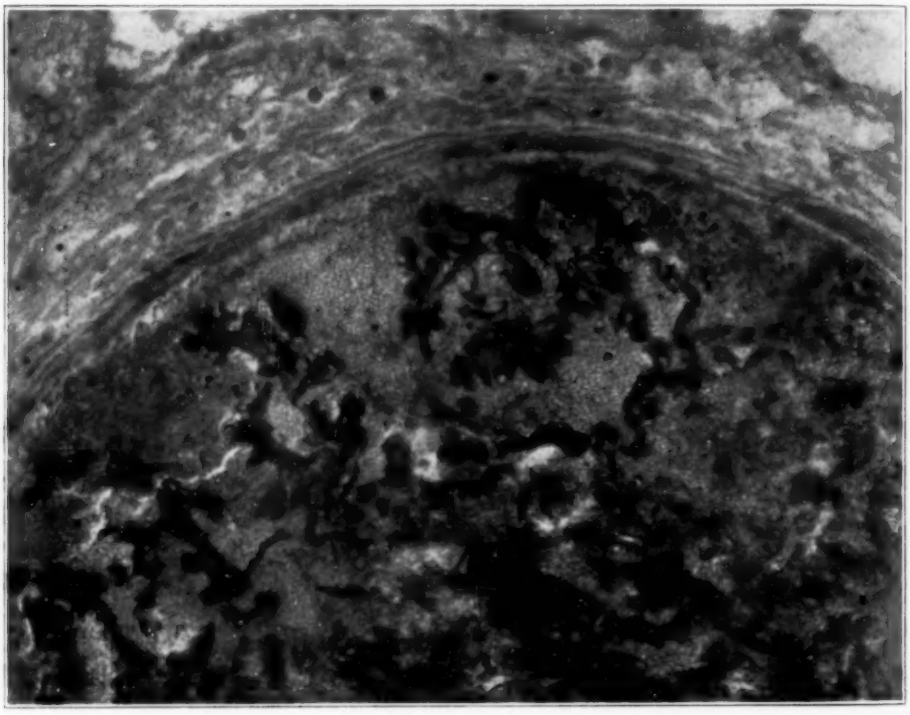

Fig. 1.—Photomicrograph of the lung from the case reported, showing foreign material and embolus in an arteriole and necroses around the vessel.

left lung was similarly bound to the wall of the chest, but the left pleural cavity contained no fluid.

The right lung weighed 922 Gm., and the left, 815 Gm. The pleural surfaces were dull and covered by numerous tags of fibrin. The lungs were dark purple, mottled here and there with pink and yellow areas. They had a liver-like consistency, and numerous nodules could be felt in the pulmonary substance. On section, the surface was dark red-brown, and there was a marked excess of bloody fluid. The tissue for a distance of 1.5 cm. inward from the pleural surface was almost black and contained numerous small yellow nodules with tiny red centers.

These nodules were from 0.3 to 1 cm. in diameter and were present in the deeper parts of the lungs also.

The diagnosis at autopsy was bilateral pneumonia, and this was recorded on the death certificate, but microscopic examination proved it to be incorrect.

TABLE 1.—*Summary of Forty-Nine Cases Reported* *

	Drug		
	Arsphenamine	Neoarsphenamine	Salyrgan
Number of cases	36	12	1
Per cent of all cases	73.47%	24.49%	2.04%
Range of dose in Gm.	0.4 - 0.6	0.3 - 0.9	1 cc.
Time of onset	1 min. to 5 hr.	1 min. to 24 hr.	Immediate
Signs and symptoms			
Dyspnea	81.57%	90.00%	
Cyanosis	78.94%	90.00%	
Cough	78.94%	90.00%	100.00%
Bloody sputum	5.26%	30.00%	
Pain in chest	62.65%	90.00%	100.00%
Fast pulse	18.42%	90.00%	
Fever	23.68%	20.00%	
Leukocytosis	23.68%	10.00%	
Physical signs of pneumonia	23.68%	10.00%	
Shock	16.00%		
Epigastric pain	5.26%		
Vomiting	16.00%		
Died	81.57%	80.00%	100.00%
Time until death	1 min. to 40 days	40 min. to 40 hr.	Immediate
Lived	18.43%	20.00%	
Autopsy performed	7.89%	60.00%	
Pulmonary edema	.....	50.00%	
Pulmonary infarct	33.33%		
Pulmonary abscess	.....	16.66%	
Pulmonary embolism	66.66%	33.32%	
Per cent of cases due to embolism as shown by symptoms or by autopsy	84.21%	100.00%	100.00%

* The cases summarized here were reported by the following authors: Blanton, W. B.: Four Fatalities Following Salvarsan, Am. J. Syph. **3**: 648, 1919. Busman, G. J., and Woodburne, A. R.: Acute Arsphenamine Collapse, Report of Case, ibid. **14**: 477, 1930. Deerop and Salle: Arsphenamin in Morocco, Ann. d. mal. vén. **18**: 897, 1923. Hart, C.: Ueber den Salvarsan-Gehirntod, Med. Klin. **18**: 444, 1922. Hedge, H. M.: Sudden Death from Arsphenamin, Illinois M. J. **48**: 157, 1925. Kiner, G.: Death after Neo-Arsphenamin Injection, Ugesk. f. laeger **87**: 415, 1925. Laurent, C.: Six années de thérapeutique par les novarsénobenzènes, Ann. d. mal. vén. **20**: 801, 1925. Laurentier, C.: Intoxications et morts par les arsénobenzènes—leur cause, Ann. de dermat. et syph. **1**: 38, 1921. Maerz, F.: Salvarsan Beschädigungen, München. med. Wehnschr. **71**: 943, 1924. Phelps, J. R.: A Fatal Case of Acute Poisoning by Neoarsphenamin, U. S. Nav. M. Bull. **22**: 217, 1925; Reactions Incidental to Administration of 191,778 Doses of Neo-Arsphenamin and Other Arsenicals, ibid. **27**: 208, 1929. Ravaut, P.: Les accidents produits par les novarsénobenzénes, Ann. de dermat. et syph. **2**: 494, 1921. Scott, E., and Moore, R. A.: Fatalities Following the Use of Arsphenamin, J. Lab. & Clin. Med. **13**: 345, 1928. Sussig, L.: Zu den Todesfällen nach Salvarsanbehandlung, Med. Klin. **17**: 1082, 1921. Weiss, S.: A Clinical Investigation of Arsphenamin Poisoning, J. A. M. A. **84**: 577 (Feb. 21) 1925. Werthern, A. M.: Salvarsanbeschädigungen, Klin. Wehnschr. **3**: 627, 1924. Widal, F.: Infarctus pulmonaire post-arsénobenzolique; infection latente par le "Perfringens," Bull. Soc. méd. d. hôp. de Paris **49**: 912, 1925. Wolf, I. J., and Bongiorine, H. D.: Sudden Death with Salyrgan, Canad. M. A. J. **25**: 72 1931. Wood, C. I.: Report of a Fatal Case of Acute Poisoning by Neo-Arsphenamin, U. S. Nav. M. Bull. **27**: 505, 1929.

Microscopically, the lungs presented the following picture: Most of the tissue was consolidated and congested. The nodules consisted of areas of necrotic tissue surrounded by zones of leukocytes and erythrocytes. In the center of the necrotic areas were arterioles filled with a network of green-yellow-brown, hyalin-like material arranged in whorls and embedded in thrombi composed of fibrin, erythrocytes, leukocytes and nuclear débris. The appearance is shown in figure 1.

A diagnosis of foreign body embolism of the pulmonary arterioles, with multiple abscesses of the lungs, was made.

Subsequent Findings.—An investigation was undertaken to see if the patient had received intravenous medication prior to admission to the hospital. A conference with his physician revealed that the history given at the hospital was incorrect, and that the sequence of events was as follows:

On Oct. 1, 1931, the patient consulted the physician because of a small sore on the glans penis. A diagnosis of herpes was made, but when there was no improvement by October 6, the physician advised the patient to take syphilitic treatment without delaying for a Wassermann test. An injection of 0.9 Gm. of neoarsphenamine dissolved in distilled water was administered.

Immediately after the injection, the patient remarked: "That certainly did hit me in the chest! It is hard to breathe." The physician thought the reaction was purely psychic and sent the patient home, but that night he was called to see him and found symptoms of pneumonia. When there was no improvement by October 9 he sent him to the hospital.

Apparently no error in technic was made, and several patients had received injections from the same box of the drug with no unusual symptoms. An ampule of the same lot was secured for experimentation.

The speed with which the symptoms developed after the injection and the microscopic observations leave no doubt that this was a case of pulmonary embolism from neoarphenamine.

Table 1 has been compiled from the data in the forty-eight cases reported in the literature and the case reported here. It is notable that the four most outstanding symptoms in these cases were sudden pain in the chest, dyspnea, cyanosis and cough. These are typical symptoms of pulmonary embolism.

PATHOLOGY OF EMBOLISM FROM DRUGS

The essential pathologic lesion in these cases is a foreign body embolism of the pulmonary arterioles, although similar emboli have been reported in other organs, and I have found them in the liver and kidneys.

In all the experimental cases, there is found a peculiar appearance of the endothelial cells of the arterioles of the lungs. The cells are apparently raised from the media of the vessel, and they seem to bulge out into the lumen. This is probably due to a high concentration of the drug at that point.

In patients who die from injections of neoarsphenamine or arsphenamine, the lumens of the pulmonary arterioles contain thrombotic masses varying from yellow-green to brown. These masses are arranged in a whorling manner, and for the most part are homogeneous and hyalin-like in appearance, although here and there may be seen an occasional erythrocyte or a vacuole resembling an erythrocyte. The appearance of these emboli can be seen in figure 1.

In the cases of embolism from injections of sulpharsphenamine, the emboli resemble coiled strands of fibrin, which look like skeins of yarn, and pink-staining granular material.

The plugging of the arterioles with these drug-protein emboli results in an infarction of the region supplied by the vessel and also in a toxic action on the surrounding tissues. Any one who has been unfortunate enough accidentally to inject arsphenamine or neoarsphenamine into the tissues knows the marked local reaction and necrosis which occur, and it seems certain that the presence of high concentrations of these drugs in the pulmonary arterioles must produce marked toxicity in the surrounding tissues and resulting necrosis.

If the patient survives the immediate shock of the accident, the areas around these vessels undergo necrosis, and multiple abscesses are formed throughout the lungs. While no work has been done on other organs in this experiment, emboli have been found in the liver and kidneys, and it is interesting to speculate that perhaps the nitritoid crises, acute atrophy of the liver and arsenical encephalitis may be due to similar emboli lodging in the brain and other organs. This is pure speculation, and it is hoped that future work may be directed along these lines.

AIMS OF THIS EXPERIMENT

Having reviewed the literature, and being impressed by the number of deaths from this cause and also with the great diversity of theories, I undertook this work in an attempt to solve the following problems:

1. Will some of the commonly used drugs produce pulmonary embolism when administered intravenously?
2. What is the most plausible theory in regard to the formation of the emboli?
3. Is a change in the p_H value of the drug responsible? If so, how small a change is necessary to cause embolism?
4. Is it possible to prevent these reactions? If so, how?
5. Is it possible to cure a patient with this type of embolism?

EXPERIMENTAL DATA

Detection of Arsenic in Lungs.—Portions of the lungs of the patient in the case reported were macerated and digested; the organic matter was destroyed, and the residue tested for arsenic by the Marsh test. No trace of arsenic was demonstrable, and colorimetric tests for arsphenamine were equally unsuccessful. The accuracy of the tests in this case was questionable.

Drugs Tested.—Following the aims of the experiment, the following arsenical drugs were employed: neoarsphenamine, arsphenamine, sulpharsphenamine, silver arsphenamine and sodium cacodylate. In addition, the following nonarsenical drugs were also tested: salyrgan, sodium iodide and a 50 per cent solution of dextrose.

Precipitation of Drugs in Vitro.—Knowing that other workers had been able to produce precipitation of arsphenamine in serum in vitro by changing the p_H value of the drug, I undertook an experiment to determine whether a change in the p_H value of other drugs would also cause precipitation when the drugs were added to serum in test tubes. If so, it would be possible to determine how much change in the degree of acidity or alkalinity would be necessary to cause precipitation.

The drugs were dissolved in distilled water and brought to a certain p_H value by means of buffer solutions. The buffer solutions used were the phosphate buffers prepared according to the methods described in Mathew's "Physiological Chemistry." The drugs were then added to test tubes containing dog's serum, and the presence or absence of a precipitate was noted.

TABLE 2.—*Effect of p_H on Precipitation of Drugs in Serum in Vitro*

p_H	Arsphenamine	Neoarsphenamine	Sulpharsphenamine	Salyrgan
1.0	++++*	++++	++++	++++
2.0	++++	++++	++++	++++
3.0	++++	++++	++++	++++
3.2	++++	++++	++++	++++
3.5	++++	++++	++++	++++
3.8	++++	++++	++++	++++
4.1	+++	++++	++++	++++
4.4	+++	++++	+++	+++
4.7	+++	+++	+++	+++
5.1	++	++	++	—
5.4	++	++	++	—
5.6	++	+	+	—
5.8	+	+	+	—
6.1	+	+	+	—
6.4	+	+	—	—
6.7	—	+	—	—
7.0	—	—	—	—
7.3	—	—	—	—
7.6	—	—	—	—
7.9	—	—	—	—
8.2	—	—	—	—
8.5	+	—	—	—
9.1	++	—	—	—
9.8	++	—	—	—
10.0	+++	—	—	—
10.7	++++	—	—	—
11.2	++++	—	—	—
11.7	++++	—	—	—

* ++++ = strong coagulation; +++ = heavy flocculation; ++ = flocculation; + = slight flocculation. The serum is of p_H 7.5.

The results of this experiment can be seen in table 2. The drugs were precipitated in serum in the following manner: arsphenamine of p_H 1 to 7 and of p_H 8.5 to 11.7; neoarsphenamine of p_H 1 to 7; sulpharsphenamine of p_H 1 to 6.1, and salyrgan of p_H 4.4. to 4.7. At values below p_H 4.4, salyrgan was precipitated from solution before it was added to serum. Silver arsphenamine was precipitated from solution

if the p_H value of the solution fell below 7 or was higher than 7.3. For this reason, no solution of the drug could be obtained to test with serum. Dextrose, sodium iodide and sodium cacodylate did not yield precipitates.

To check the p_H value of the solutions, the buffer phosphate and acetate solutions described in Mathew's "Physiological Chemistry" were used with appropriate indicators.

The question arose as to whether the acidity of the solutions was precipitating the proteins of the plasma without any action on the part

TABLE 3.—*p_H of Drugs Examined in These Experiments*

Drug	Number Ampules	Manufacturer	p_H	Comment
Neoarsphenamine.....	22	A	7.3	
Neoarsphenamine.....	1	A	5.4	Drug produced embolism when injected into rabbits
Neoarsphenamine.....	1	A	6.4	Drug produced embolism when injected into rabbits
Neoarsphenamine.....	11	B	7.3	
Neoarsphenamine.....	1	B	6.4	Drug produced embolism when injected into rabbits
Neoarsphenamine.....	1	C	7.3	Drug from same lot as that given in the case reported in this article
Arsphenamine.....	12	A	4.1	Before alkali
Arsphenamine.....	12	A	7.9	After alkali
Sulpharsphenamine.....	12	A	5.6	
Silver arsphenamine.....	6	B	7.3	
Salyrgan.....	10	B	7.4	
Sodium cacodylate.....	6	D	7.4	
Sodium iodide.....	6	E	7.4	
Neoarsphenamine.....	1	A	5.8	Drug produced embolism when injected into rabbits. Drug detected in outpatient department by dye method
Neoarsphenamine.....	1	A	6.1	Drug produced embolism when injected into rabbits. Drug detected in outpatient department by dye method
Neoarsphenamine.....	1	A	6.1	Drug produced embolism when injected into rabbits. Drug detected in outpatient department by dye method
Neoarsphenamine.....	1	A	5.8	Drug produced embolism when injected into rabbits. Drug detected in outpatient department by dye method

of the drugs, and so the various buffer solutions were added to the serum. No precipitate occurred, showing that the process was not a coagulation of the plasma proteins by acid.

The procedure outlined in table 2 was repeated, a synthetic serum prepared by dissolving albumin in Ringer's solution being used. Identical results were obtained with this synthetic serum and with dog's serum, thus eliminating any possibility of a specific erythrocyte-protective action on the part of the plasma proteins.

P_H of Drugs Used.—The next step was to determine the p_H of the drugs as normally present in ampules obtained on the market. A large number of ampules of the drugs were tested, and the different values found are recorded in table 3. A specimen of neoarsphenamine

from the same box as that used in the case reported here was found to be of a neutral p_H and did not produce embolism when injected into rabbits.

TABLE 4.—*Effect of p_H of Drug on Production of Pulmonary Embolism in Rabbits*

Rabbit*	Dose, Gm.	p_H	Symptoms	Embolism
			Arsphenamine	
A 1	0.1	3.2	Sudden death with dyspnea	Yes
A 2	0.1	4.1	Sudden death with dyspnea	Yes
A 3	0.1	5.4	Dyspnea, cyanosis, died 10 hours	Yes
A 4	0.1	6.4	Dyspnea, cyanosis, died 21 hours	Yes
A 5	0.1	6.7	None	No
A 6	0.1	7.0	None	No
A 7	0.1	10.0	Dyspnea, cyanosis, slow respiration	No
A 8	0.1	7.3	None	No
			Sulpharsphenamine	
S 1	0.1	3.2	Sudden death with dyspnea	Yes
S 2	0.1	5.8	Dyspnea, cyanosis, died 9 hours	Yes
S 3	0.1	6.1	None	No
S 4	0.1	6.4	None	No
S 5	0.1	7.3	None	No
			Neoarsphenamine	
N 1	0.1	3.2	Sudden death with dyspnea	Yes
N 2	0.1	3.4	Sudden death with dyspnea	Yes
N 3	0.1	4.7	Dyspnea, cyanosis, died 24 hours	Yes
N 4	0.1	5.4	Dyspnea, cyanosis, died 26 hours	Yes
N 5	0.1	6.1	Dyspnea, cyanosis, died 28 hours	Yes
N 6	0.1	6.4	Dyspnea, cyanosis, died 26 hours	Yes
N 7	0.1	6.7	None	No
N 8	0.1	7.0	None	No
N 9	0.1	9.8	None	No
N 10	0.1	10.7	Dyspnea, cyanosis, slow respiration	No
N 11	0.1	7.3	None	No
N 12	0.1	7.3	None	No
N 13	0.1	6.4	Dyspnea, cyanosis, died 10 hours	Yes
N 14	0.1	6.4	Dyspnea, cyanosis, died 20 hours	Yes
N 15	0.1	5.8	Dyspnea, cyanosis, died 5 hours	Yes
N 16	0.1	6.1	Dyspnea, cyanosis, died 11 hours	Yes
N 17	0.1	6.1	Dyspnea, cyanosis, died 10 hours	Yes
N 18	0.1	5.8	Dyspnea, cyanosis, died 1 hour	Yes

* A 8 received arsphenamine combined with bromthymol blue.
S 5 received sulpharsphenamine combined with bromthymol blue.
N 4 received spoiled neoarsphenamine (manufacturer A).
N 11 received neoarsphenamine combined with bromthymol blue.
N 12 received neoarsphenamine from same lot as received by patient in case reported.
N 13 received spoiled neoarsphenamine (manufacturer A).
N 14 received spoiled neoarsphenamine (manufacturer B).
N 15 received spoiled neoarsphenamine (manufacturer A).
N 16 received spoiled neoarsphenamine (manufacturer A).
N 17 received spoiled neoarsphenamine (manufacturer A).
N 18 received spoiled neoarsphenamine (manufacturer A).

Precipitation of Drugs in Vivo.—As it had been found that the drugs would precipitate in serum in vitro if the solution was acid, they were brought to a definite p_H value by means of the phosphate buffer solutions and were then injected into the veins of the ear of a rabbit.

The results of these injections can be seen in table 4. In every case the presence or absence of embolism was determined by microscopic examination of the lungs.

Injections of acid solutions of salyrgan, sodium iodide, sodium cacodylate and dextrose did not result in embolism or death. The absence of embolism was proved by microscopic section of the lungs.

COMMENT

As can be seen from the experimental data, precipitation occurred whenever arsphenamine, neoarsphenamine, sulpharsphenamine or salyrgan was brought to certain p_H values below neutral and then added to serum in test tubes. This showed definitely that a change in the p_H of the drugs would cause a precipitate, and also showed the change necessary to bring this about.

The serum had been repeatedly centrifugated, and contained few if any erythrocytes. In spite of this fact, precipitation occurred, showing that the precipitate and the embolism produced were not due to hemolysis of erythrocytes, as is maintained by some workers.

In order to rule out any possible connection with erythrocytes, a synthetic serum was used in the experiments, and identical results were obtained, thus proving that in this work at least the precipitation was not due to hemolysis or to agglutination of erythrocytes.

The question was raised as to whether the precipitate could be due to a coagulation of the plasma proteins by the acidity of the solutions added. This was disproved by a failure of the precipitate to occur if the acid solutions were added to serum, even if the p_H of the solution was as low as 1.

Precipitation of acid solutions of arsphenamine have been observed since the first work of von Meissner, but the precipitation of neoarsphenamine and of sulpharsphenamine has been disputed by many workers. Schamberg [19] said: "There is no evidence that neo-arsphenamin is ever precipitated in the blood as no one has ever been able to produce emboli." Kolmer [25] made the following statement: "Solutions of neo-arsphenamin sulpharsphenamin and tryparsamide do not coagulate proteins when added to serum in test tubes even when equal parts of concentrations as high as 10% isotonic solutions and serum are mixed. . . . . As manufactured at present, neo-arsphenamin produces no visible changes in serum in vitro and there is no reason at all for assuming that coagulation of proteins occurs in vivo when this drug is injected intravenously even in concentrated solutions."

25. Kolmer, J. A.: Chemotherapy with Special Reference to Treatment of Syphilis, Philadelphia, W. B. Saunders Company, 1926, p. 588.

Contrary to the findings of these men, this work has shown that acid solutions of neoarsphenamine and of sulpharsphenamine will cause a precipitate when added to serum in vitro. In addition, spoiled ampules of drug, that is, samples with a low p_H value, will cause a precipitate in serum if added in the same manner in which they would be injected.

Why other workers have been unable to produce this precipitate is a mystery. The reason may be that they used hydrochloric acid to acidify their solutions while in this work sodium hypophosphate and sodium acid phosphate combinations have been used to obtain the desired p_H. These substances are normal blood buffers, and so cannot be considered as foreign substances. Except in the case of arsphenamine, precipitates could not be produced in this experiment if hydrochloric acid was used to acidify the solutions. Apparently, the drugs undergo some chemical change with hydrochloric acid which prevents the process of coagulation.

Oliver and Douglas [20] as well as Jeanselme and Pomaret [17] have shown conclusively that the precipitate consists of both the drug and protein. Kolmer [25] has demonstrated that when acid arsphenamine is added to serum, the resulting precipitate removes 35.1 per cent of the serum albumin and 30.7 per cent of the serum globulin. This indicates that there is some combination between the drug and the proteins of the blood which causes the precipitate. What this combination is is unknown. Some believe that the reaction is one of mechanical adsorption, and others believe that it is a chemical combination. So far, no definite proof has been offered for either theory as it is a very difficult problem to determine whether there is a loose capillary attraction between the two substances or whether a new chemical compound is formed.

Evidence points toward the theory of chemical combination and this seems to be the more plausible one, especially if one accepts the "iso-electric point theory," as advanced by Hunter and Patrick.[26] This theory involves the difficult field of colloidal chemistry, and makes a simple explanation very difficult. However, a few definitions and well established facts will be presented in order to make the matter as clear as possible.

The "iso-electric point" of a solution is the hydrogen ion concentration at which the particles migrate neither to the anode nor to the cathode, and the solution is ionized equally as an acid and as a base. Hunter and Patrick [26] have shown that this point is p_H 3.39 for arsphenamine, and that the region of precipitation extends from p_H 3 to 10.5.

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26. Hunter, A. S., and Patrick, W. A.: Studies on the Physical and Colloidal Chemistry of Arsphenamin, J. Lab. & Clin. Med. **10**:446, 1925.

The particles of a colloidal solution are known as "micelles." The micelle is a type of ion with an accumulated charge and is intermediate between the molecule in chemistry and the cell in biology. In some respects it possesses the properties of the molecule, and in other respects the properties of the cell.

Hunter and Patrick have shown that arsphenamine is a colloidal substance, and their investigation indicates that the cause of the precipitation in serum is some such mechanism as the following: If an

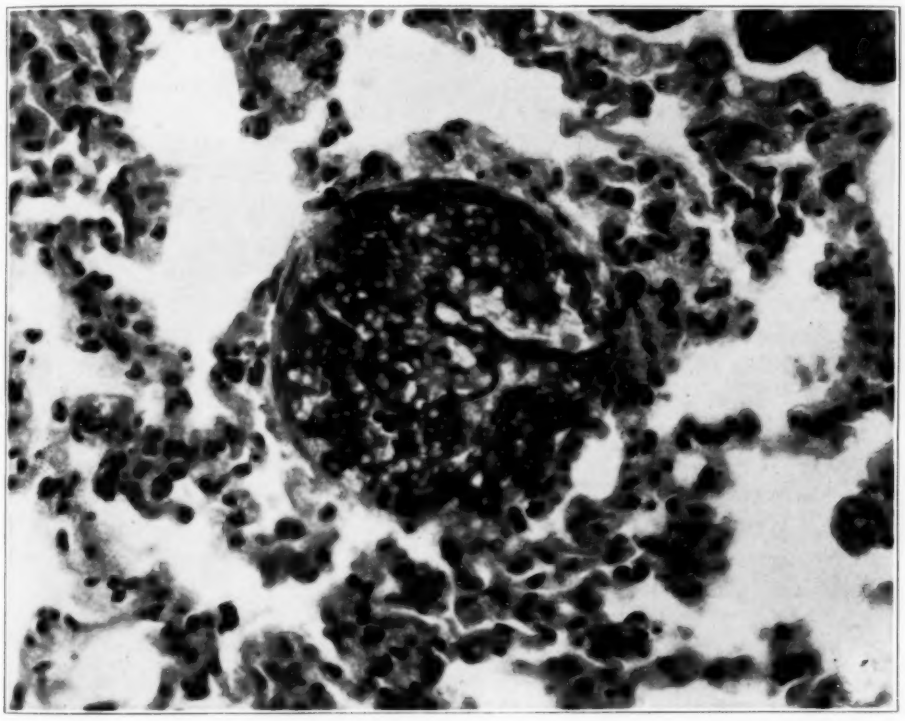

Fig. 2.—Photomicrograph of an arteriole in the lung of a rabbit, showing an embolus formed by precipitation of neoarsphenamine.

acid solution of the drug is introduced into the blood, the buffers of the blood immediately attempt to bring the solution to the normal p_H of the blood. In this process, the drug is carried through a point at which the conductivity of the solution drops to a point characteristic of the molecular form of the drug; the ionic micelle, being in a physical state suitable for union with some substance, joins with the proteins of the blood, and a precipitate results. It is possible that union exists at other p_H values, and that precipitation occurs only if the p_H of the drug

drops to the point at which the drug and protein complex cannot remain in solution.

Neoarsphenamine has been shown to exhibit colloidal properties, and this mechanism probably applies to it and to sulpharsphenamine as well as to arsphenamine.

This "iso-electric point theory" is at present the most plausible explanation for the precipitation of these drugs in serum, and my opinion is that the substance formed is either a protein arsphenamine or an arsphenamine proteinate, probably the same as the "proteinophenolic complex" described by Jeanselme and Pomaret.[17]

As can be seen in table 4, whenever arsphenamine, neoarsphenamine or sulpharsphenamine was injected into animals, the drug being in the p_H range for precipitation, the animals died with symptoms of embolism, and at autopsy the pulmonary arterioles contained emboli.

The failure of other workers to produce embolism with neoarsphenamine may be due to some factor in their method of acidification. This work has shown, beyond doubt, that these three forms of arsphenamine will produce embolism when injected in acid solution. In evidence of this, there is a case in which death resulted from an injection of neoarsphenamine, and there were numerous cases of experimental embolism in rabbits, as the table shows.

In cases of drug embolism in human beings, the patient experiences sudden, severe pain in the chest and becomes dyspneic and cyanotic. The pulse becomes rapid, and a state of collapse occurs. Owing to the asphyxia resulting from bronchial and alveolar compression with impaired ventilation, circulatory failure and paralysis of the respiratory center occur. If the stage of immediate collapse is survived, the condition develops into an embolic pneumonia, as described by Swerdtfeger and Tinker[27] and by Loeb,[28] with leukocytosis, fever, bloody sputum and signs of pulmonary consolidation or multiple abscesses. If the patient is fortunate, recovery may occur. Statistics indicate that the mortality is 80 per cent.

As has been brought out earlier in this report, at a conservative estimate there are about 800 deaths a year in the United States from arsenical drugs administered intravenously, and a considerable percentage of these deaths are due to pulmonary embolism. Very few cases have been reported, but no doubt many physicians can recall cases in which immediate collapse or pneumonia followed an injection, and death was not reported as being due to the arsenical. In most cases, the physicians probably do not connect the death with the injection. The

27. Swerdtfeger, O., and Tinker, M.: Pneumonia Following Injections of Arsenobenzol, Am. J. Syph. **3**:398, 1919.

28. Loeb, H.: Salvarsantod und Grippe, Arch. f. Dermat. u. Syph. **138**:253, 1921.

ease with which this error may be made is illustrated in the case reported here. If an autopsy had not been performed, the case would no doubt have been recorded permanently as one of pneumonia.

Since arsphenamine has been used less and physicians have turned to the use of neoarsphenamine, they have felt that they had a drug which was practically harmless. It is this idea that I wish to correct. From the observations in this work, neoarsphenamine is very dangerous, in fact more dangerous than arsphenamine, since the latter is carefully alkalinized before injection and there is no check on the reaction of the neoarsphenamine used.

The following statements in support of this fact are taken from the report of the British Medical Research Council in 1922:[29]

> No special arsenobenzol preparation can be regarded as more likely to produce ill effects than others. Errors in technic can not account for more than a few serious accidents as fatalities occur in the most carefully controlled clinics. A feeling among clinicians that neoarsphenamin is a very much milder drug than arsphenamin and consequently can be given in larger doses and more frequently is not justifiable. In regard to the nitritoid crises, there is much evidence connecting them with the physical properties of the drug, their association with rapidly precipitating solutions of old salvarsan, imperfectly soluble specimens and acid arsphenamin. Such observations and the usually rapid evanescence of the symptoms seem to clearly show that we are dealing with a phenomenon which has no connection with the presence of arsenic in the molecule but is the result of the disturbance in the colloidal condition of the blood.

It is definitely known that injections of acid solutions of arsphenamine, neoarsphenamine and sulpharsphenamine will cause the formation of a precipitate in the blood which will result in pulmonary embolism. There is also considerable support in the literature for the fact that the nitritoid crisis may also be due to tiny emboli lodging in the brain and spinal cord and resulting in hemorrhages and toxic actions on the vital centers.

With these facts in mind and with the knowledge that at best there is 1 death for every 16,000 injections, the matter assumes an important aspect.

The drug companies have endeavored to standardize their preparations so that these accidents cannot occur, but they have failed. Examinations of boxes of an apparently satisfactory drug with a p_H value of about 7.3 have shown that there is occasionally an ampule with a p_H of from 5.4 to 6.4, and injection of these acid preparations into rabbits has resulted in embolism. If they had been injected into human beings, embolism would no doubt have occurred. The fault cannot be that of the manufacturer, since each batch of drug is tested on animals for toxicity before it is put up in ampules. However, after it leaves the

29. Medical Research Council: Toxic Effects Following the Employment of Arsenobenzol Preparations, Brit. M. J. **2**:184, 1922.

factory, something happens. Perhaps one ampule in a lot of the drug will undergo some form of deterioration which results in a fall of its p_H value into the precipitation zone. An injection of such a spoiled drug may cause death. It is impossible for a manufacturer to be able to tell ahead of time that a certain ampule will deteriorate. What the nature of the deterioration is is not known. It is not always due to air leaking into the ampules, since the ampules detected in this work were air-tight. The answer as to why the whole batch does not deteriorate awaits further investigation.

No physician knowing the foregoing facts, especially that only one ampule in a batch may be spoiled, and that this ampule may cause death, can inject these drugs into patients without concern. One must have drugs with which to treat syphilis, and these preparations have proved to be of definite value, but no physician would like to know that one of his patients died as a result of an injection which he had administered, nor does he wish to be constantly in dread of such an occurrence every time he administers the drugs.

MEANS OF PREVENTION OF DRUG EMBOLISM

The means of prevention of embolism due to drugs are as follows: First, one must exercise the utmost care in the preparation of the drugs for injection. They should be dissolved in triple distilled water and should never be heated or shaken, as an increase in toxicity is apt to occur.

Second, no acid or alkali should be added to the drugs before injection, except in the case of arsphenamine, which, according to the directions, requires the addition of a specific amount of alkali.

Third, the drug should be injected very slowly in order to keep the concentration in the vein at a minimum. Many workers have shown that rapid injection increases the likelihood of precipitation because of the high concentration of the drug in the vein. Many of the patients who survive may owe their recovery to the slowness with which the drug was injected.

Fourth, great care should be used not to give too large a dose. It is notable that in the cases reported in the literature 20 per cent of the patients received a dose of 0.75 Gm. and 60 per cent received 0.9 Gm. In other words, 80 per cent received more than the conventional 0.6 Gm. This fact substantiates a report made by the Cologne Commission [3] that when the dose of neoarsphenamine is increased from 0.6 to 0.9 Gm., the ratio of death rises from 1 for 11,289 injections to 1 for 3,000.

Fifth, there is a means of prevention which was devised as a result of this work, and which will unquestionably prevent any reactions due to precipitation of the drug in the blood. This will eliminate pulmonary

embolism and may perhaps prevent many of the nitritoid crises, if they are due to tiny emboli, as some believe.

SPECIAL METHOD OF PREVENTION

With the idea of determining a method for the prevention of the accidents due to changes in the p_H of the drugs, an investigation of various indicator dyes was made, for it was felt that if an indicator could be combined with the drugs to show the p_H, it would be possible to avoid the injection of an acid solution.

After examination of several indicators, bromthymol blue was selected. Its chemical designation is *di*-bromthymol-sulphonphthalein, and being a sulphonphthalein dye it is closely related to phenolsulphonphthalein and *tetra*-iodophenolsulphonphthalein which are commonly used for tests of the kidney and gallbladder.

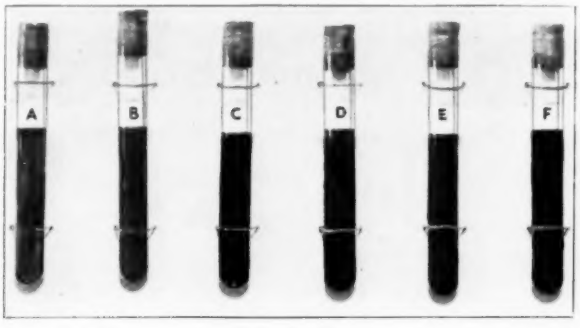

Fig. 3.—Series of tubes containing 0.6 Gm. neoarsphenamine and 0.0008 Gm. bromthymol blue, showing the absence of any green color below p_H 7; tube *A*, p_H 6.4; *B*, 6.7; *C*, 7; *D*, 7.3; *E*, 7.6, and *F*, 7.9.

Bromthymol blue has a p_H range from 6 to 7.8 and is yellow on the acid side and blue on the alkaline side. It was found to have a very sharp end-point at p_H 7 when combined with neoarsphenamine, in which case it gives a green solution if alkaline and a yellow solution if acid. This sharp change in color is illustrated in figure 3. The amount of dye which must be combined with the drug to give a satisfactory color is 0.8 mg. per ampule of drug.

Pharmacology of Bromthymol Blue.—It having been found that the dye was satisfactory as an indicator when combined with drugs, the next step was to determine its toxicity. As can be seen in table 5, a rabbit weighing 2 Kg. can receive 500 mg. of the dye without serious consequences. A rabbit of similar weight was killed by an injection of 800 mg. The dye is eliminated chiefly through the kidneys, although

some may be eliminated through the gallbladder. The dye was not opaque and so did not show up in roentgenograms.

When it had been determined that a rabbit could stand with impunity a dose of 500 mg., or 625 times the dose advocated for use with the drugs, the dye was combined with each drug to see if the combination of the two was toxic for rabbits. The results showed no evidence of toxicity.

Since there were no bad results in rabbits from injection of the dye and drugs, a human being was given 0.8 mg. of bromthymol blue intravenously. No symptoms developed. Following this, people received injections of neoarsphenamine combined with 0.8 mg. of the dye. Up to the time of writing, 64 injections of this combination have been made into human beings. No ill effects have been noted. During this period, four ampules of drug with a p_H value below neutral were discovered

TABLE 5.—*Toxicity of Bromthymol Blue for Rabbits*

Dose, Mg.	Weight, Gm.	Symptoms	Autopsy Observations
0.4	2,500	None	None
0.8	2,340	None	None
2.0	2,200	None	None
4.0	1,970	None	None
40.0	2,060	None	None
100.0	1,870	None	None
500.0	2,200	Iris became blue; conjunctivae, tip of nose and mucous membranes turned green; for twenty-four hours thick dark green urine passed; within eight hours nose and mucous membranes were of normal pinkness; iris also pink; rabbit as lively as normal; killed on the seventh day	None
800.0	1,890	Rabbit had convulsions and death resulted	None

by means of the dye. When these were injected into rabbits, pulmonary embolism occurred, as proved by autopsy.

It is my belief that the addition of 0.8 mg. of bromthymol blue to each ampule of dry drug will prevent the occurrence of reactions due to precipitation of the drug in the blood, not by preventing the deterioration of the drug, but by providing a way in which the physician, at the time he prepares the drug for injection, can himself determine whether it is too acid for use. If, on making up the drug in distilled water, he finds that the resulting solution is yellow instead of green, he can be sure that the p_H of the drug is below p_H 7 and is probably in the danger zone of precipitation, and that the preparation is apt to kill if injected.

It has been shown that the dye is not toxic for rabbits in a dose 625 times the amount advocated for use with the drugs. It has been shown that the dose recommended is not toxic alone or in combination with drugs, either for rabbits or for man. It has also been shown that even in large doses there is no resulting pathologic lesion in the kidneys or liver of rabbits.

Therefore, if the dye is not toxic and if it will afford protection against the injection of a spoiled ampule of drug, it should certainly be used. Any means that will prevent a single death a year, let alone hundreds, is one which physicians cannot but demand that the manufacturers employ, as a protection both to the patients and to themselves.

The question has been raised as to whether this method can be used without the actual introduction of the dye into the patient. It can. By putting two drops of a 0.04 per cent solution of bromthymol blue in a test tube and adding five drops of the solution prepared for injection, a green color results if the drug is satisfactory for injection and a yellow color if the drug is too acid.

As far as can be determined, there is no objection to the injection of the dye with the drug, and the incorporation of the dye in the ampule at the time of manufacture to avoid the necessity of adding it at the time the drug is prepared for injection has definite advantages. If the dye is placed in the ampule with the drug, in a dry state, there is no opportunity for the dye to deteriorate and lose its indicating properties. The greatest advantage is that any physician, no matter how remote from drug stores, can always tell if the drug is too acid for use.

If, on the other hand, the dye must be added at the time of injection, there are several disadvantages. The physician giving an occasional dose of neoarsphenamine may not have any of the dye available at the time, or he may be so far from a large pharmaceutic house that he cannot delay long enough to secure it. Second, solutions of the dye kept for a long time undergo some evaporation with a change in the concentration of the dye and a resulting error in the test.

In 1928, Chambers [30] advised using phenolphthalein with arsphenamine to prevent the injection of an acid solution. This method is satisfactory for arsphenamine, since most of the solutions of arsphenamine have a p_H of about 7.9 after alkali has been added, and the end-point of phenolphthalein is at p_H 8. Phenolphthalein is red below p_H 8 and colorless above this point. However, in the case of neoarsphenamine, this indicator would not be satisfactory, since most of the ampules of neoarsphenamine have a hydrogen ion concentration of from p_H 7 to 7.3. As phenolphthalein takes on a red color at values below p_H 8, its use with neoarsphenamine would result in the discarding of practically all ampules of the drug. This is not true of bromthymol blue, as its end-point is at 7 when combined with neoarsphenamine.

TREATMENT OF PATIENTS WITH DRUG EMBOLISM

In the event that a physician has an accident with the drugs as they are available now, what is to be done?

30. Chambers, S. O.: An Aid in the Prevention of Acid Arsphenamin Administration, J. A. M. A. **91**:320 (Aug. 14) 1928.

The patient should immediately be treated for shock, with lowered head, heat and morphine, if the pain is severe. Epinephrine hydrochloride in a dose of 5 minims (0.3 cc.) of a 1:1,000 dilution, should be administered intravenously, followed by an intramuscular injection of 1 cc. of the same dilution. It appears that sodium thiosulphate, in 15 grain (1 Gm.) doses, given intravenously, has a marked action in decreasing the toxicity of drug emboli and in hastening their absorption. According to McBride and Dennie,[31] the beneficial action is due to the fact that it converts the arsenical drugs to a nontoxic insoluble sulphide. The patient should receive one dose of thiosulphate intravenously at once, and this dose should be repeated daily until no signs of reaction remain. If embolic pneumonia occurs, symptomatic treatment, counter-irritation and the administration of sodium thiosulphate and of oxygen seem to be the only methods which are of value. Statistics indicate that in 20 per cent of the cases of accidents the patients may recover.

SUMMARY

1. A case in which death resulted from an injection of neoarsphenamine is reported, and a summary is given of 47 cases of accidents from arsenical drugs and a case of death from salyrgan reported in the literature.

2. Statistics show that about 800 deaths from these drugs occur annually in the United States.

3. A large part of the deaths are due to pulmonary embolism resulting from a combination of the drugs with the plasma proteins.

4. An acid reaction of the drug, as indicated by a p_H value below 7, appears to be the cause of the precipitation of the drug in the blood.

5. If the p_H of the drugs is below 7, neoarsphenamine, arsphenamine, sulpharsphenamine and salygran will precipitate in dog's serum in vitro.

6. If the p_H of the drugs is below 7, neoarsphenamine, arsphenamine and sulpharsphenamine will precipitate in rabbit's serum in vivo, causing pulmonary embolism.

7. A method is outlined whereby the combination of bromthymol blue with the drugs in ampules will enable the physician to determine, at the time of injection, whether the drug is suitable for administration.

8. A plan of treatment for use is outlined when accidents result from injections of acid solutions of these drugs.

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31. McBride, W. L., and Dennie, C. C.: Treatment of Arsphenamin Dermatitis and Certain Other Metallic Poisons, Arch. Dermat. & Syph. **7**:63 (Jan.) 1923.

ASYMPTOMATIC SYPHILIS

EFFECT OF VARIOUS DRUGS ON SPIROCHAETA PALLIDA IN THE BRAINS OF RABBITS AND MICE

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While the rabbit is an animal well adapted for chemotherapeutic studies in syphilis, nevertheless, when one is concerned with drugs intended for the treatment of dementia paralytica, the usefulness of the rabbit for the testing of the efficiency of such drugs is definitely limited by the fact that the spirochetes of syphilis are ordinarily unable to penetrate into the central nervous system of the rabbit, or to persist there for appreciable periods of time if directly introduced (Levaditi and his associates [1] and Raiziss and Severac [2]). Even with animals displaying severe generalized lesions, with the infection running a course of several years, in some cases, it is impossible to discover any spirochetes in the brain either by means of a direct microscopic observation or by inoculation of emulsified brain substance into the testes of normal rabbits.[2b] Only a few cases have been reported in the literature in which spirochetes have been found in the central nervous system of the rabbit, and these must be regarded as exceptional (Brown and Pearce,[3] Plaut and Mulzer,[4] Hoffmann and Strempel [5] and Uhlenhut and Mulzer [6]).

The experimental work was done at the Dermatological Research Laboratories.

Read before the Section on Dermatology and Syphilology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 12, 1932.

1. Levaditi, C.; Lépine, P., and Schoen, R.: Etude pathogénique expérimentale de la parasyphilis, Compt. rend. Soc. de biol. **109**:86, 1932.

2. Raiziss, G. W., and Severac, M.: (*a*) Testicular Lesions in Rabbits Following Intraspinal Syphilitic Infection, Proc. Soc. Exper. Biol. & Med. **24**:756, 1927; (*b*) Chemotherapeutic Studies Concerning the Penetration of Organic Compounds of Arsenic into the Cerebrospinal System, Arch. Dermat. & Syph. **22**:1031 (Dec.) 1930.

3. Brown, W. H., and Pearce, L.: Syphilitic Infection of Central Nervous System of Rabbit, Arch. Dermat. & Syph. **2**:635 (Nov.) 1920.

4. Plaut, F., and Mulzer, P., cited by Mulzer: Morphologie und Biologie der Spirochaeta pallida experimenteller Syphilis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, p. 187.

5. Hoffmann, E., and Strempel, R.: Dermat. Ztschr. **56**:1, 1929.

6. Uhlenhut, P., and Mulzer, P., cited by Mulzer.[4]

A development of considerable interest, and one which promises to be of importance for the chemotherapeutic study of syphilis, was inaugurated by the discovery by Kolle and Schlossberger [7] that mice and rats, previously thought to be immune to the syphilitic virus, are capable of harboring an asymptomatic syphilitic infection which may be rendered manifest by inoculation of emulsified organs of the mice or rats into the testes of normal rabbits, in which, in a large percentage

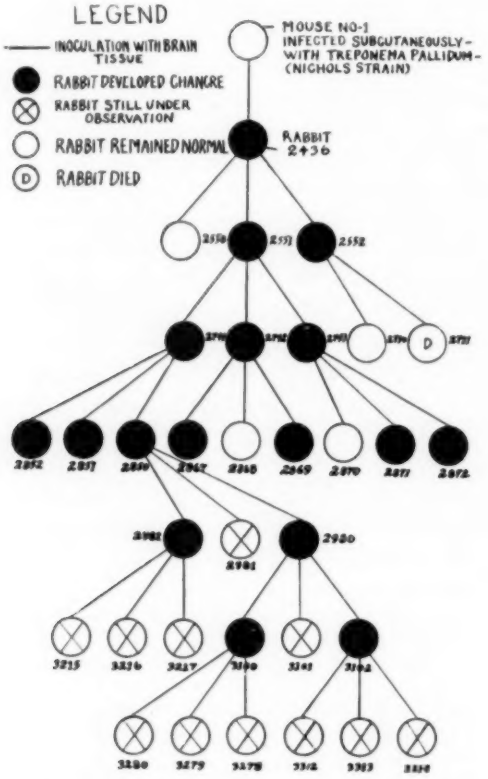

Fig. 1.—Diagram representing five passages of spirochetes through rabbits infected originally with the brain of a syphilitic mouse and subsequently with rabbits' brains, showing the acquired ability of Spirochaeta pallida to penetrate into the brains of rabbits.

of cases, well defined lesions abounding in spirochetes subsequently develop. Perhaps the most interesting feature of these experiments

7. Kolle, W., and Schlossberger, H.: Experimentelle Studien über Syphilis und Rekurrensspirochätose: V. Ueber symptomlose Infektion von Mäusen und Ratten sowie symptomlose Superinfektionen syphilitischer Kaninchen mit Spirochaeta pallida, Deutsche med. Wchnschr. **52**:1245, 1926; Die Persistenz der Syphilisspirochäte in Mäusen während langer Zeiträume, ibid. **54**:129, 1928.

was the fact that the brains of the infected mice were shown to be virulent in equal measure with the other organs. These new facts were immediately utilized for the chemotherapeutic study of drugs intended for the sterilization of the central nervous system by treating mice harboring an asymptomatic syphilitic infection with such drugs, and then observing whether the brains of mice so treated retained their virulence or became sterile. A more detailed discussion of these experiments, with references to the literature, will be found in a previous article.[8] This article is, however, principally concerned with a still further development, which also forms the starting point of the present investigation.

It was soon found by Schlossberger that the brains of rabbits in which lesions had developed in consequence of inoculation with brain emulsion of mice or rats harboring an asymptomatic syphilitic infection

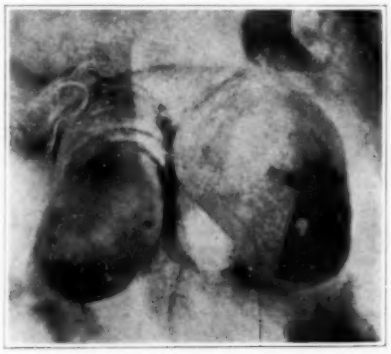

Fig. 2 (rabbit 2851).—Testicular chancres containing numerous active spirochetes obtained as a result of inoculation with brain substance of a syphilitic rabbit (third passage). The starting point in this series was the brain of a syphilitic mouse.

also became virulent, as shown by the inoculation of emulsion made from them into the testes of normal rabbits. Thus it was demonstrated that the spirochetes, apparently as a result of their sojourn in the brain of the mouse, had acquired the property of neurotropism, i. e., the ability to penetrate into the central nervous system of the rabbit, and to persist and multiply there. It was shown by Schlossberger,[9] and also

8. Raiziss, G. W., and Severac, M.: Neurotropism of the Spirochaeta Pallida: Experimental Studies with Special Reference to the Asymptomatic Syphilis of Mice, Arch. Dermat. & Syph. **26**:271 (Aug.) 1932.

9. Schlossberger, H.: Experimentelle Untersuchungen über das Eindrigen der Syphilisspirochäten in das Zentralnervensystem von Mäusen und Kaninchen, Arb. a. d. Staats-Inst. f. exper. Therap., 1928, no. 21, p. 344; Ueber das Verhalten der Syphilisspirochäten im Mäuseorganismus bei Passagen, Med. Klin. **25**:307, 1929.

by us in the article cited, that such a strain can be carried through several successive passages from rabbit to rabbit without losing its neurotropic properties; our experiments in this direction are still being continued; five passages have already been made, and so far there is no indication that such a strain cannot be carried on from rabbit to rabbit indefinitely without losing its property of neurotropism. The results of these experiments are schematically represented in figure 1. The virulence of the infection is illustrated by figures 2 and 3, which are photographs of chancres obtained in the third and fourth passages, respectively.

It has occurred to us that a possibility was here presented for a new chemotherapeutic method of studying the effectiveness of drugs intended to attack the spirochete in the nervous system. Certain advantages of the rabbit over the mouse for investigations of this nature,

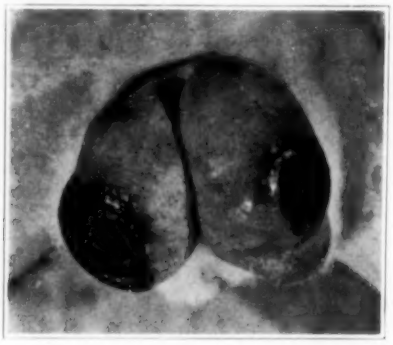

Fig. 3 (rabbit 2982).—Testicular chancres containing numerous active spirochetes obtained as a result of inoculation with brain substance of a syphilitic rabbit (fourth passage). The starting point in this series was the brain of a syphilitic mouse.

since it has now been found that both are capable of harboring spirochetes in the central nervous system, are immediately obvious. In the first place, the infection in the rabbit, accompanied as it is by generalized lesions, is more typical than the merely asymptomatic infection of the mouse, and thus it more nearly approaches the conditions existing in syphilis in human beings. Second, the rabbit is a much larger animal, and it is, therefore, possible to introduce the drugs that are being tested intravenously; this is the method followed in the treatment of dementia paralytica, and hence, again, the clinical conditions are more nearly approximated. Finally, a large number of mice must be used in any one experiment, since intercurrent deaths are fairly frequent, while rabbits are less susceptible to accidental influences.

METHOD

In our experiments the mice were infected in the following manner: The testes of a rabbit bearing a large chancre which contained numerous active spirochetes was removed under sterile conditions, and the chancrous tissue was excised and minced into a very fine mass to which 5 cc. of sterile salt solution was added to render the minced tissue aspirable into a Luer syringe with a metal tip to which a large needle was attached (13 gage, 1 inch [2.5 cm.] length); 0.2 cc. of the resulting semiliquid mass was usually injected subcutaneously into the back of the mouse.[10] It will be noted that this procedure differs from the original technic of Schlossberger, who infected the mice by introducing a piece of chancre under the skin of the back. Our technic was designed with a view to bringing the maximum number of spirochetes into as close a contact as possible with the body tissues of the mouse, and the uniformly satisfactory results that we have obtained seem to justify this procedure. Six weeks or more after the mice were infected, the brains were removed, minced, emulsified and injected into the testes of normal rabbits. As soon as lesions were observed to appear, the animals were treated with the drug under consideration, since it had been previously shown that spirochetes appear in the brain of the rabbit simultaneously with the appearance of testicular lesions. The brain of the treated rabbit[11] was then removed, emulsified and inoculated into the testes of normal rabbits. The entire brain of the treated animal had to be used in order that no spirochetes should escape detection, and the resulting amount of emulsion was so large that three rabbits were necessary for each brain, and injections had to be made into both testes of each rabbit. If these animals remained normal, the drug was judged to be effective, while if lesions appeared, it was concluded that the drug had failed to destroy the spirochetes present in the brain of the rabbit that was treated. We have noted that it appears to be preferable to remove the brain of the rabbit within about thirty days after treatment, since after that period the percentage of positive results seems to decrease whether the animal has been treated or not, and there is, therefore, danger in ascribing a greater efficacy to the drug which has been used than has actually been operative if too long a period has elapsed between the treatment and the removal of the brain. However, spirochetes have been shown to be present in the brain of rabbits in some cases as late as ninety-two days after inoculation, so that complete clarity on this point must await further experimental study.

RESULTS

The compounds so far studied are: arsphenamine, neoarsphenamine, sulpharsphenamine, tryparsamide and acetarsone. The results are summarized in the accompanying table.

An examination of the table shows that large doses of arsphenamine, neoarsphenamine and other chemotherapeutic agents apparently destroy the spirochetes in the brain of the rabbit, since the inoculation of the brain emulsion of rabbits so treated into the testes of normal animals yields negative results. Thus, when normal rabbits were inoculated intratesticularly with the brain emulsion of rabbits treated, respectively,

10. The opening is closed with a Michel clip to prevent escape of the emulsion.

11. The term "treated" rabbit is used to indicate that the animal received an injection of the chemical compound that was being tested.

with a single dose of 50 and 75 mg. of neoarsphenamine, no lesions were observed to appear in the first case after ninety-two days, and in the second case, after seventy days. While these results may not be considered final, since spirochetes sometimes appear in the testes of the inoculated rabbit after a long period of time has elapsed since the inoculation, nevertheless, it seems plausible to conclude that a single dose of 75 or 50 mg. of neoarsphenamine per kilogram results in a com-

Therapeutic Effect of Various Drugs Given Intravenously to Rabbits Inoculated Intratesticularly with Brain of Syphilitic Mice

Rabbit's Number	Chemical Compound	Dose per Kilogram of Body Weight	Number of Injections Given	Number of Days After Treatment When Brain and Popliteal Nodes Were Removed From the Rabbit	Results Obtained from Intratesticular Inoculation of Rabbit's			
					Brain		Popliteal Node	
					Positive	Negative Days	Positive	Negative Days
2902	Neoarsphenamine	0.050	1	31	..	92	..	..
2900	Arsphenamine	0.020	1	28	..	92	..	..
2899	Tryparsamide	0.100 0.200	1 1	31	Large node +4*	..	..	..
2951	Arsphenamine	0.010	1	33	Large superficial chancre	..	Medium node; medium chancre +4	..
2954	Sulpharsphenamine	0.025	1	28	..	84	..	..
2976	Sulpharsphenamine	0.025	1	35	..	70	..	..
2971	Tryparsamide	0.300	1	36	..	73	..	..
2962	Neoarsphenamine	0.075	1	39	..	70	..	..
2959	Acetarsone monosodium	0.125	1	36	..	73	..	..
2955	Sulpharsphenamine	0.040	1	28	..	70	..	..
2916	Acetarsone monosodium	0.100	2	28	..	86	..	..
2908	Sulpharsphenamine	0.025	1	37	..	84	..	..
2949	Acetarsone monosodium	0.025	10	47	..	73	..	..
2993	Neoarsphenamine	0.075	1	68	..	56	..	..

* +4 indicates the presence of numerous active spirochetes in the testicular lesions.

plete sterilization of the brain of the rabbit. The same effect was obtained with a single dose of 20 mg. of arsphenamine. Other chemotherapeutic agents, administered in large doses, also appear either to have checked the activity of the spirochetes in the brain or to have completely destroyed them. A single dose of 10 mg. of arsphenamine per kilogram, however, failed to sterilize the brain of the rabbit, for when it was removed and an emulsion was prepared and injected into the testes of a normal animal, a large superficial chancre appeared at the site of inoculation, although no spirochetes could be detected. The inoculation of normal animals with an emulsion made of the popliteal

nodes of the same animal resulted in the appearance of a medium node and a medium chancre on the right testis of one of the rabbits containing active spirochetes.

It is seen, therefore, that the minimum effective dose of arsphenamine for the sterilization of the brain of rabbits lies between 20 and 10 mg. per kilogram; while the true figure falls certainly within this range, the exact value will have to be obtained by further experimentation. It is not possible to deduce the minimum effective doses for neoarsphenamine and sulpharsphenamine from these experiments, since the doses employed were in all cases sufficient to produce sterilization. In the case of neoarsphenamine, single doses of 75 and 50 mg. per kilogram were given, resulting in the sterilization of the brain; hence, the minimum therapeutic dose is certainly less than 50 mg. Similarly, it must be less than 25 mg. for sulpharsphenamine, for single doses of 25 and 40 mg. were effective.

In the case of tryparsamide, much larger doses were required to produce sterilization than with the trivalent arsenicals such as arphenamine, neoarsphenamine and sulpharsphenamine. Thus, rabbit 2899 received two doses of tryparsamide, one of 100 mg. and another of 200 mg. When the emulsion prepared from the brain of this rabbit was inoculated into the testes of a normal animal, a large initial lesion developed, containing active spirochetes; thus it is seen that the two doses of tryparsamide which were administered failed to sterilize the brain of the rabbit. However, the same amount of tryparsamide given to another rabbit as a single dose caused the spirochetes to disappear from the brain, at least so far as one may be permitted to judge from observations to date; whether this amount is a definitely sterilizing dose remains, however, to be established. In any case, it appears that very large doses of tryparsamide are necessary to produce a therapeutic effect, and of all the compounds studied, tryparsamide thus seems to be the least effective.

It is interesting to note that in rabbit 2899 the popliteal nodes were negative, while the brain was positive. It is seen, therefore, that in this case, while the popliteal nodes were sterile, spirochetes were present in the brain. Hence, in dealing with spirochetes which have passed through the body of a mouse and have, as a consequence, become neurotropic, the popliteal node test, ordinarily regarded as conclusive, must in all cases be supplemented by the brain test.

Acetarsone, another pentavalent arsenical, administered intravenously, has so far proved to be effective in smaller doses than are necessary with tryparsamide. Sterilization of the brain was obtained with a single dose of 125 mg. per kilogram, with two doses of 100 mg. and with ten small doses of 25 mg. each; acetarsone, therefore, has shown in these experiments a definite superiority over tryparsamide.

It will be noted that these results confirm the data which we have previously obtained in a study of the penetration of organic compounds of arsenic into the cerebrospinal system, in which a different method was used.[2b] A suspension of spirochetes was introduced into the subarachnoid space of the rabbit and the compound being tested was given intravenously two hours later. A dose of 300 mg. of tryparsamide did not prevent the spreading of a generalized syphilitic infection; in this animal there subsequently developed small nodes in the testes, a discharge from the nose containing spirochetes and a small ulcer on the nose. An animal treated with 100 mg. of acetarsone, however, remained normal for twenty weeks of observation, at the end of which its popliteal nodes were transferred to normal animals; the latter remained normal for eight months of observation.

CONCLUSIONS

1. The spirochete of syphilis, as a result of a sojourn in the organism of the mouse, acquires the property of being able to penetrate into the brains of rabbits. Our experiments show that this characteristic property is retained after as many as five successive passages, the brain of the rabbit having been employed each time as the source of spirochetes. This series of passages is at present being continued.

2. When rabbits are inoculated with such a neurotropic strain, the appearance of spirochetes in the brain is simultaneous with the appearance of the testicular lesions. It is not certain, however, that the spirochetes remain in the brain of the rabbit for long periods of time.

3. A new chemotherapeutic method for the study of the penetration of antisyphilitic remedies into the central nervous system has been devised by us, and has been applied in the study of arsphenamine, neoarsphenamine, sulpharsphenamine, tryparsamide and acetarsone

4. The procedure is, briefly, as follows: An emulsion of the brain of a syphilitic mouse is injected intratesticularly into rabbits; when lesions containing large numbers of active spirochetes appear, the rabbits are treated intravenously. The brain of each animal is removed from thirty to sixty days, preferably thirty, after treatment, and three normal rabbits are inoculated intratesticularly with the emulsion prepared from this brain in order to determine the sterilizing properties of the chemical compound that has been used.

5. As a preliminary result of this study, it appears that tryparsamide requires large doses for the sterilization of the brain, while acetarsone and arsphenamine with its derivatives require smaller doses for a similar therapeutic effect.

J. C. Moetsch of the Dermatological Research Laboratories, Philadelphia, cooperated with us in this work.

ABSTRACT OF DISCUSSION

DR. EARL D. OSBORNE, Buffalo: I read this paper with a great deal of interest. I think it is the first attempt to use a method whereby drugs can be tested for their action on neurosyphilis after development of conditions in animals closely simulating those in the human body. We have pointed out many times that the estimation of the arsenic content of the spinal fluid is a poor means of determining the therapeutic efficiency of any arsenical. Dr. Raiziss has been exceedingly conservative in the claims he has made. In his paper he points out the pitfalls of assuming any superiority for any particular drug on the work he has done. Obviously, he has just begun, and must carry out many more experiments to determine the minimum effective dose of any drug. So far as his experiments have gone, they seem to indicate that arsphenamine is the most effective of the trivalent chemicals and that acetarsone is more effective than tryparsamide. I sincerely hope he will be able to carry on this work, for I am sure that all those who are interested in the treatment of neurosyphilis feel that tryparsamide leaves much to be desired.

I shall be greatly interested to know whether Dr. Raiziss is able to carry the neurotropic strain from rabbit to rabbit indefinitely. From my work, I doubt whether this neurotropic strain can be propagated in this way indefinitely, although Dr. Raiziss is of the opinion that it can be. After all, it is the soil in which the spirochete grows that is the greatest factor. Otherwise, how can we explain that the passage of the strain through the brain of the mouse produces a neurotropic strain in the rabbit? How long this strain can continue this ability will be interesting to observe.

In the paper, Dr. Raiziss pointed out the criticisms that are always present in work on rabbits. He has been perfectly frank about them. The soil is different than in the human being. There is not the long-existing infection that is present in the human being in dealing with neurosyphilis, which is important in evaluating any particular arsenical in the treatment of neurosyphilis.

DR. HAROLD N. COLE, Cleveland: I should like to ask whether Dr. Raiziss examined other organs for Spirochaeta pallida besides the testes and the brain.

DR. JEFFREY C. MICHAEL, Houston, Texas: I should like to know whether the strain with which Dr. Raiziss is working originated from neurosyphilis in a human being.

DR. J. P. THORNLEY, New York: If I did not misinterpret the paper, the original strain was obtained from the mouse, in which animal the brain is uniformly involved in all kinds of syphilis. It is interesting to note that clinical observers in France claimed, and Marie still does, I think, that there was a definite neurotropic strain of the spirochete. There was the classic illustration of the three men, all of whom got their infection from the same source, and in all of whom dementia paralytica developed. Is it not possible that once in a while the spirochete encounters a human brain which is easily invaded, and that a neurotropic strain is then and there developed?

This is one of the most interesting papers that I have listened to in a long time.

DR. FRANK W. CREGOR, Indianapolis: In regard to the penetrability of the trivalent as compared with the pentavalent arsenicals, I should like to have Dr. Raiziss bring that work up to date for us.

DR. GEORGE W. RAIZISS, Philadelphia: In regard to the question raised by the illuminating discussion of Dr. Osborne, he emphasized that the host plays an important part in the penetration of the spirochete into the brain. Our experiments have shown the reverse; i. e., that the ordinary strain does not penetrate

into the brain of the rabbit, while in the case of the specific neurotropic strain, which is obtained by only one passage through a mouse, there is definite evidence of the penetration of the spirochete into the brain. Apparently, the spirochete has definitely changed since the same species of animals has been employed. Therefore, it is the spirochete which is predominantly, if not exclusively, responsible for this penetration, and not the host.

I was asked what is the origin of our so-called normal strain. The normal strain that we employ was originally isolated by the late Major Nichols, who obtained it from a patient with dementia paralytica and then passed it through rabbits. We have employed it in our laboratory for nearly twelve years, carrying it from rabbit to rabbit. We have already subjected the ordinary strain to hundreds of passages, and we have never been able to find that the strain penetrated into the brain of a rabbit.

In answer to the question concerning the origin of the strain, the spirochete is first taken out of the rabbit and passed once through the mouse, and it is then available as a neurotropic strain.

Answering the question of Dr. Cole, we have found that we can obtain Spirochaeta pallida not only from the brain of the mouse, but from various of its organs. We have obtained the spirochete from the liver, popliteal lymph nodes and spleen.

In regard to the correlation of our present findings with those that I reported two years ago, the experiments have not progressed sufficiently for me to make such correlation.

We have two groups of arsenicals, pentavalent and trivalent. While the pentavalent arsenicals penetrate into the cerebrospinal system in larger amounts than the trivalent, unfortunately, they are less spirocheticidal than the latter. If we ever find a chemical compound that will penetrate into the brain in larger quantities, and which, on the other hand, is a highly spirocheticidal agent, a most difficult therapeutic problem will be solved.

A PSORIASIFORM ERUPTION WITH PUSTULAR EXACERBATIONS

MICHAEL H. EBERT, M.D.
CHICAGO

From time to time during the past five years we have had the opportunity to observe an unusual type of eruption in two sisters who have been patients of Dr. Oliver S. Ormsby, through whose courtesy this study has been made possible. The disorder dates back to childhood in both cases, with periods of marked activity at irregular intervals.

REPORT OF CASES

Case 1.—*History.*—Mrs. D., of American birth and German descent, was born in 1902. Her first cutaneous trouble appeared at the age of 2 months as a generalized, bright red exanthem, which suggested prickly heat. At 6 months this became exfoliative and persisted until 2 years of age. From the age of 4 years to 12 years she had four similar attacks, each lasting several months. When 15 years of age, discrete psoriasiform lesions appeared for the first time on the elbows, the trunk and the scalp. Later the scalp became pustular, and the condition eventuated in exfoliative dermatitis, with which she was confined to bed for one and one-half years. Her physician gave her solution of potassium arsenite, and within three months her skin was practically clear. She took arsenic continuously, in large doses, for the next eight years, and when first seen, she had arsenical keratoses of the palms and soles. She was then free from cutaneous trouble with the exception of two attacks of general dermatitis, one precipitated by the use of Stillman's freckle cream and the other by the use of a solution of mercuric chloride. In the autumn of 1926, psoriasiform plaques again appeared on the elbows and the back and persisted until March, 1927, when they were aggravated by the application of chrysarobin.

Observations.—While the patient was under our observation, the disorder presented three fairly distinct phases.

The Interim Phase: During this phase the patient was relatively free from the disease. Only a few resistant psoriasiform plaques were present on the extensor surface of the arms, and on the back and the legs, with a more or less patchy scaling in the scalp. Latterly, the nails were also involved.

The Subacute Phase: This phase usually appeared in the winter or early spring and gradually increased in intensity. From March, 1927, to March, 1932, the patient had seven such attacks of several months' duration, characterized by a marked activity of the disorder. All of the attacks occurred in the late winter or early spring months, with the exception of one, which took place in the autumn of 1929. The following description is characteristic of this phase, and a

Read at the Fifty-Fifth Annual Meeting of the American Dermatological Association, Havana, Cuba, May 5, 1932.

similar condition has been observed many times. During some of the attacks the lesions beneath the breasts and in the crotch were moist, and at other times the lesions on the legs suggested an infectious dermatitis.

On March 29, 1932, the patient had her usual late winter exacerbation, which had started in January and slowly increased in intensity. In the twenty-four hours preceding her admission, many of the plaques, particularly the larger ones, developed an inflammatory areola and became tender and painful, while many new pustules appeared at the periphery of these plaques and in some instances in the

Fig. 1 (case 1).—Subacute stage, illustrating the distribution.

erythematous areola about the plaques. She complained of a chilly sensation and some malaise.

At the time of admission to the hospital, there were several types of lesions.

(*A*) Scattered over the trunk and extremities were many discrete papules, varying in size from that of a pinhead to that of a large match-head. The smaller ones appeared to be follicular; the larger ones were flat-topped and covered with a silvery, imbricated scale which was easily removed and exposed a dry, flat, pinkish papule. This type of lesion had appeared gradually since January, and showed no evidences of inflammatory reaction.

(*B*) There were plaques varying in size from that of a coin to that of a hand. These were well defined, slightly raised and covered with a silvery scale or with

a crusting scale of a slightly yellowish tinge. In the larger lesions the scale was unevenly distributed over the surface. Between the scales the plaque was covered with a transparent film through which could be seen flat, intra-epidermal lakes of pus, the majority being the size of a pinhead, but some being irregular in outline and from 2 to 4 mm. in the long axis. Many of these plaques, especially the larger ones, were surrounded by an inflammatory areola, from ½ to 1 inch (1.27 to 2.5 cm.) wide, and over the hips this areola was also closely set with numerous minute, intra-epidermal pustules. The lesions felt hot and were tender. The distribution of the larger plaques on the extensor surface of the arms, over the buttocks and on the thighs and legs (fig. 1) was similar to that seen in psoriasis.

(*C*) Under the breasts and about the vulva the plaques were more moist and of the intertriginous type.

(*D*) There were three dry, scaly plaques, the size of a quarter, on the butterfly area of the face. This was the first appearance of the disorder on this locality.

Fig. 2 (case 1).—Subacute stage, showing distortion, distal separation and subungual keratosis of the finger-nails; there are a few scaling patches on the backs of the hands.

Similar lesions occurred behind the ears and in the concha of the ears, and were of exactly the type of psoriasis seen associated with arthritis.

(*E*) All of the nails were involved (fig. 2). They were rough, thickened, without luster, separated distally and undermined with a moist, keratotic material, and in places with small lakes of pus. The interdigital spaces on the feet were macerated.

(*F*) There was dry, coarse, patchy scaling throughout the scalp; in places the scale mounted on the hair shafts.

The Acute Phase: During a period of subacute activity of the type just described, there suddenly appeared, while the patient was under our observation at the Presbyterian Hospital, a period of much more acute and intense activity. Without apparent cause malaise, chills, fever up to 101 F. and a leukocytosis of 15,000 developed. The plaques became inflammatory, and a wide erythematous areola appeared about them. Numerous transient, miliary, intra-epidermal pustules appeared on their surface and in the surrounding areola. Other areas of the body,

the palms, the soles and the buttocks, became red, edematous and painful and were the site of recurrent crops of ephemeral pustules of the same type. Soon the skin over the entire body became swollen, red and painful; the face was swollen. The condition seemed about to terminate in generalized exfoliative dermatitis. However, within ten days of its onset it subsided as rapidly as it had appeared, leaving only a few residual psoriasiform plaques. Blood cultures made during the height of activity and the inoculation of material from the pustules on aerobic and anaerobic mediums and at various oxygen tensions proved negative, as did autoinoculation experiments and inoculation of the contents of the pustules into animals.

The patient gave a history of having had similar acute attacks on other occasions, always as a terminal event of the subacute phase.

The terminal inflammatory stages of the subacute phase are undoubtedly abortive manifestations of the acute phase and have frequently occurred.

The past history revealed nothing of importance with the exception of an attack of polyarthritis in the spring of 1931, which lasted about ten days and was relieved by salicylates. This attack was followed by an acute exacerbation of the cutaneous trouble.

The patient had been married eight years previously, and had never been pregnant. Physical examination revealed no significant findings except a relatively low blood pressure, 105 systolic and 70 diastolic, and a scrotal type of tongue, which was also present in her sister (case 2). All other examinations, including tests of the basal metabolism, chemical analysis of the blood, a Wassermann test and urinalysis, gave negative results.

Family History.—The father died at 40 years of age of dropsy. The mother was 72, and was well. She had been married two times. By her first husband she gave birth to two boys and two girls. One boy was drowned, and the other was living and well and had two healthy children. One girl died in infancy; the other was well, married and the mother of three healthy children. By her second husband, the patient's mother gave birth to four girls. They were all living and all married and none had borne children. The patient, who was the youngest, and her sister, who is the patient in our case 2 and the second child, are the only ones in the family who had any cutaneous trouble.

Histopathology.—On April 9, 1930, a biopsy specimen was taken from a match-head-sized, flat papule located over the right scapula. The surface was dry and pinkish and was covered with a silvery scale. Clinically, the condition was psoriasis. This represents the type of lesion present during the interim phase of the disorder.

Under a low power lens, the heaped up scale was seen to be from five to six times the width of the epidermis and was made up of alternating lamellae of keratin and lenticular masses of pyknotic round cell nuclei. Acanthosis was marked. The rete pegs were broad, flat and edematous. The papillae did not approach the surface. There were micro-abscesses in the upper rete. The cellular infiltrate was confined to the edematous papillary and subpapillary layers of the corium.

Under a high power lens (fig. 3), nucleated and nonnucleated lamellae were seen to alternate in the stratum corneum of the epidermis. Lenticular masses of pyknotic polymorphic nuclei lay between the planes of the lamellae. These masses were formed by the serial exfoliation of micro-abscesses. The stratum granulosum was absent in some areas and present in others. The rete mucosa was edematous. Micro-abscesses were found in three stages of their evolution.

In the first stage, over the edematous papillae there was a marked emigration of polymorphonuclears through the dilated spaces between the edematous rete cells.

In the upper layers the rete cells were much flattened into a reticulum, in the interstices of which were accumulated polymorphonuclears. This was an early subcorneal micro-abscess (fig. 3*A*).

In the second stage, the subcorneal abscess was more distinct. It was densely packed with polymorphonuclears, and the reticulum was less evident. In this stage the emigration of leukocytes in the lower rate was not marked (fig. 3*B*).

In the third stage, a flattened mass of pyknotic polymorphonuclears was being excreted between the lamellae of the stratum corneum (fig. 3*C*).

There was some edema of the papillary layer of the corium, with dilatation of the capillary loops and the lymph spaces. There was a moderate round cell infiltrate which was limited to the papillary and subpapillary layers. It consisted prin-

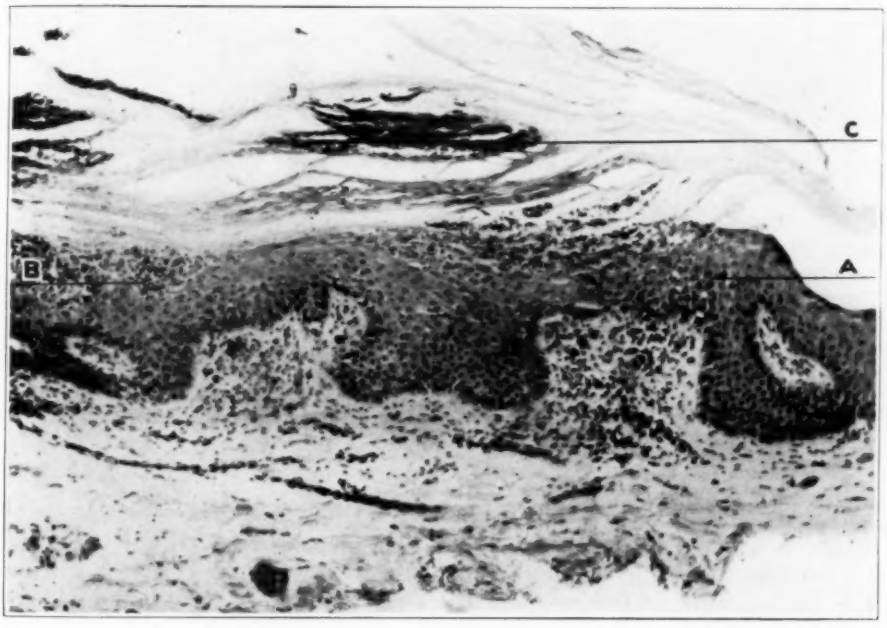

Fig. 3 (case 1).—Subacute stage. Section from a match head-sized, flat-topped, dry papule covered with a silvery scale, located on the scapula. *A* shows the migration of polymorphonuclear leukocytes from edematous papillae into the subcorneal spaces between the flattened rete cells; *B*, densely packed subcorneal micro-abscess; *C*, exfoliating micro-abscess; × 110.

cipally of reticulo-endothelial cells, lymphocytes and swollen connective tissue cells. A few polymorphonuclears were present in the papillae. There were no changes in the elastica or the appendages of the skin, and there was little pigment in the basal layer.

A second biopsy specimen was taken during an acute stage of the disease from a small papule of a few days' duration on the right shin. It was inflammatory and contained three small lakes of pus. Under a low power lens the epidermis was seen to be diffusely thickened and edematous. At one end of the section a spherical micro-abscess had been exfoliated and appeared as a shrunken mass of pyknotic nuclei in the scale. The upper third of the corium was edematous, and there was a moderate papillary and subpapillary round cell infiltrate.

Under a high power lens a moderate amount of thickening of the stratum corneum made up of lamellae of keratin was seen. These thickenings were nucleated in only a few areas. The stratum granulosum was well developed except near the micro-abscess and beneath the exfoliated pyknotic nuclei. In general, the rete cells were edematous and the rete pegs were acanthotic, but in no place did the papillae approach the surface closely. Micro-abscesses could be seen in various stages of development.

In the first stage, over a papilla there was an intense intercellular and intracellular edema of the rete cells, with reticular degeneration of some of these cells. Others were compressed to form a reticulum, the interstices of which were filled with polymorphonuclears, which had emigrated from the edematous papillae below.

In the second stage, there was a well developed micro-abscess which was under tension. The floor was formed by flattened rete cells, from two to three layers thick and bulging downward in the corium. The roof projected upward and was covered with lamellar stratum corneum. The walls showed evidences of reticular degeneration, described in the first stage, with a reticulum of flattened rete cells. The center was packed with polymorphonuclears, with only a few resistant rete cells to form a reticulum.

In the third stage, lenticular masses of pyknotic polymorphonuclears were being excreted between the lamellae of the stratum corneum.

In the papillary and reticular layers of the corium there was considerable edema, with dilatation of the blood and lymph spaces. There was also a round cell infiltrate, which consisted of reticulo-endothelial cells, swollen connective tissue cells, lymphocytes and a few polymorphonuclears, which were more numerous beneath the micro-abscess. The amount of cellular infiltrate beneath the large abscesses was not nearly what one might expect. The elastica and appendages of the skin were not changed.

Case 2.—*History.*—Mrs. T., a sister of the patient in case 1, was 34 years of age. Heavy scaling appeared in her scalp at the age of 8 years and persisted until she was 16, when psoriasiform scaling plaques appeared on the back, where they were confined until she was 25 years old, when they spread to the extremities. Like her sister, she had periods of acute and subacute exacerbation. Since 1925, she gave a history of having had three acute attacks, terminating in generalized exfoliative dermatitis. The first attack started with generalized, miliary red points, which soon became pustular, and within a few days the whole body was red, swollen, painful and exfoliating. Fever ensued, according to the history, and she was confined to bed for eight months. A similar but less severe attack was precipitated by the application of chrysarobin in 1928. She was again confined to bed with a similar attack during the first four months of 1930.

She had had subacute attacks, usually in the late winter months of each year, but sometimes in the early fall. I was able to study her while she was in the hospital during these attacks.

Examination.—A general physical examination revealed no significant anomalies except a scrotal tongue. The patient was well developed and weighed 138 pounds (62.6 Kg.). The types of lesions were almost identical with those described in her sister, except that the nails were never involved and there were no intertriginous plaques.

On Oct. 3, 1929, during a subacute phase, the patient had an eruption on the scalp, trunk and extremities. Over the left thigh there were several nummular to palm-sized, round, oval or irregular, dull red plaques. The center of each plaque appeared glazed; at the periphery there was an irregular, yellowish, crusted scale. Two large plaques were present over the right hip. The right thigh presented

similar but less marked lesions. There were similar plaques on the legs. Minute intra-epidermal pustules, the size of a millet seed, flush with the surface, were present near the periphery of some of the plaques (fig. 4). On puncture, a drop of sticky, grayish-yellow pus could be extracted. When the resultant minute cavity was explored with a needle, the corium seemed spongy and covered with a firm roof, which constituted the glazed surface of the plaque. Bacteria could not be demonstrated in smears from the pus. Auto-inoculation experiments gave negative results, as did all attempts to cultivate organisms in mediums or by animal inoculation. A biopsy specimen was taken from the margin of the plaque on the right shin.

Fig. 4 (case 2).—Subacute stage. Plaque on the anterior lateral surface of the leg, showing the glazed surface and the minute intra-epidermic pustules, which are not raised, of twenty-four hours' duration.

On the back were many scaly papules, varying in size from that of a match-head to that of a split pea. The scales seemed heaped up in the central part of the papules. Similar papules were present on the extensor surfaces of the arms, especially about the elbows. The nails were normal. Patchy, adherent, psoriasiform scaling was present on the scalp, in places extending up the hair shaft. There was a little psoriasiform scaling in the concha of each ear.

Course.—From day to day, while the patient was in the hospital, one or more of the plaques became more inflammatory, developing an erythematous areola, while groups of minute intra-epidermal pustules appeared on the surface. Their contents dried within twenty-four hours and were exfoliated as a thin scale. The temperature and leukocyte count remained normal and the general condition seemed good.

During the interim between attacks, the lesions were drier, more like psoriasis, and limited to the scalp, back and extensor surface of the extremities.

Histopathology.—A biopsy specimen was taken from the margin of a chronic plaque during a period of subacute activity. The three phases in the evolution of a micro-abscess by the migration of polymorphonuclear leukocytes through the epidermis, which are described in case 1, could be demonstrated in this case.

Another biopsy specimen was taken from the margin of a more active plaque in which pustules had appeared a few hours previously. The evolution of these macro-abscesses was essentially the same as that of the micro-abscesses, except that the inflammatory reaction was well marked (fig. 5).

The nosological position of this disorder presents difficulties. A few similar cases have been described in the literature. They have been

Fig. 5 (case 2).—Subacute phase. Section taken from the margin of the patch to show the macro-abscess which had appeared in the glazed surface twenty-four hours previously; × 36.

identified with two entirely different disorders, i. e., acrodermatite continué of Hallopeau and psoriasis.

ACRODERMATITE CONTINUÉ

Hallopeau,[1] in 1890, first described a suppurative polydactylitis in a male patient with frequent exacerbations of generalized, ephemeral, small pustules. Darier found Staphylococcus albus in the original lesion. In 1892, Hallopeau[2] described a similar eruption in a psoriatic male patient 48 years of age, which was of twelve years' duration. It arose

1. Hallopeau, H.: Ann. de dermat. et syph. **1**:420, 1890.
2. Hallopeau, H.: Ann. de dermat. et syph. **3**:504, 1892.

as a suppuration following an injury to the right thumb nail and was confined to this area for two years. Later it involved both palms and all the fingers. It was characterized by the constant recurrence of superficial, ephemeral pustules, varying from the size of a pinhead to several millimeters in diameter, and level with the surrounding surface on a reddened and eroded area with an undermined margin. Jeanselme identified Staphylococcus aureus as the causal organism.

By 1897, Hallopeau [3] had observed and recorded two more cases. His idea as to the essential features of the disorder had been extended and modified, as is indicated by the change in title from polydactylitis suppurative recidivant to acrodermatite continué, for he had seen the disorder limited to one finger in one instance, and again had seen it spread beyond the fingers and toes to other areas on the hands and feet; moreover, the elementary lesions might be vesicular rather than pustular. He considered the constant recurrence of new eruptive elements the essential feature. He was still of the opinion that staphylococcus was the causal agent.

In 1901, Audry [4] summarized the known cases. He emphasized the intractability and persistence of the disorder, which is characterized in the typical case by lakes of pus and in the formes frustes by vesicles, which in either case are situated in the outer layer of the epidermis. The vesicles persist only a few hours and are exfoliated as a squama, leaving temporarily an eroded surface, but are constantly reformed. The eruption originates on the digits about the nails and is limited to the hands and feet, except in the malignant case reported by Fréche and Hallopeau, which will be described later. Some or all of the nails are constantly involved, as in an ordinary whitlow, and the involved digits are finally reduced to little conical and sclerosed stumps. Audry considered the staphylococcus as a secondary invader and the cause a neuritis.

Many later observers, including Barber and Eyre [5] in England and Sutton [6] in America, have concluded that acrodermatite continué is identical with dermatitis repens of Crocker, although there are many points of difference in the original descriptions.

In the *Annales de dermatologie et de syphiligraphic* for 1897, Fréche [7] described an eruption on the hands of a male patient, aged 42. It had originated eight months previously as a suppuration about the right thumb nail. The lesions involved successively the other nails, the

3. Hallopeau, H.: Ann. de dermat. et syph. **8**:473, 1897.
4. Audry, C.: Ann. de dermat. et syph. **2**:913, 1901.
5. Barber, H. W., and Eyre, J. W. H.: Brit. J. Dermat. **39**:485, 1927.
6. Sutton: J. Cutan. Dis. **29**:325, 1911.
7. Fréche: Ann. de dermat. et syph. **8**:491, 1897.

fingers and the palms. They were well defined peripherally by an undermined and up-turned collaret of epidermis. The surface was dull red, moist and studded with small, flat pustules. The nails had fallen, and the nail beds were purulent. The lips were crusted and the tongue grooved. Plaques covered with a diphtheritic membrane were noted on the buccal mucosa at the onset. Fréche regarded this case as an example of Crocker's dermatitis repens. After eight months of observation the patient came under Hallopeau's [8] care. Shortly afterward an acute exacerbation occurred, with fever and a rapid spread of miliary and lentil-sized pustules over the entire body. The pustules subsided in a short time, leaving foci, consisting of weeping areas in the groins and on the scrotum, as well as erythematous placards, studded with small pustules and covered with yellow crusts situated on the fingers, the abdomen and the back. The lips and chin were crusted. The original eruption involved not only the hands but the feet as well, presenting crust-covered lakes of pus of irregular shape, from 2 to 8 mm. wide, in the outer layers of the thin and reddened epidermis. Lafitte identified staphylococcus as the causal organism. Hallopeau considered this case one of acrodermatite continué with acute exacerbation and multiple foci of involvement.

Stowers,[9] in 1896, described briefly a generalized erythema occurring during the course of dermatitis repens, involving the fingers, toes, palms and soles of an elderly woman.

Strandberg [10] suggested the identity of acrodermatite continué of Hallopeau with pustular psoriasis. Like several other observers, he found the elementary pustules sterile. He described acute dissemination associated with chills and fever recurring repeatedly in a patient 40 years of age, who had suffered for fifteen years from a typical acrodermatite continué of the hands. In his second case, that of a young woman, a persistent psoriasiform eruption and acute exacerbations of generalized small pustules, associated with malaise and fever, developed in the spring and fall.

In 1930, Nicolas, Massia and Froment [11] described, in a woman of 67, what they considered a unique example of generalized acrodermatite continué of Hallopeau, for doubt had been thrown on the Fréche-Hallopeau case by Bodin,[12] who considered it an example of Duhring's disease.

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8. Hallopeau, H.: Ann. de dermat. et syph. **8**:1277, 1897.

9. Stowers: Brit. J. Dermat. **8**:1, 1896.

10. Strandberg: Acta dermat.-venereol. **6**:314, 1925.

11. Nicolas, J.; Massia, G., and Froment, R.: Bull. Soc. franç. de dermat. et syph. **37**:30, 1930.

12. Bodin, E.: Paris méd. **10**:185 (March 6) 1920.

Barber and Eyre [5] have recently recorded two instances of what they considered a generalized acrodermatite continué of Hallopeau. In both cases an injury to a nail initiated the process. In both cases the disseminated lesions were of the type one is accustomed to call infectious dermatitis. There was systemic evidence of a pyoderma. Cultures from the lesions uniformly yielded staphylococci, and the blood serum agglutinated this organism in high titer. The disorder responded rapidly to the clearing up of septic foci and treatment with autogenous vaccines.

Acrodermatite continué is a fairly clearcut clinical entity as originally described. Darier,[13] in the *Proceedings of the Eighth International Congress of Dermatology* at Copenhagen in 1930, in discussing a case presented as acrodermatite continué of Hallopeau, stated that in his opinion many distinct disorders are reported under this title. He felt that this group should be analyzed and dissociated. In order that the two cases reported may be identified as instances of a disseminated variety of this disorder, it must be shown either that they began as typical examples with later dissemination, or that during their course they presented easily recognizable features of that disease. It is for this reason that I have outlined the classic symptoms of acrodermatite continué. In addition, the histopathology must be consistent.

All the cases hitherto recorded have originated as acrodermatite continué of the hands or feet with later dissemination. The Fréche-Hallopeau case originated as suppuration about the right thumb nail, gradually involved the fingers and palm and extended to the other hand and later to the toes and soles, with pustular lesions characteristic of acrodermatite continué. Acute dissemination occurred only after two years. Nicolas and his associates described the disorder appearing as a *mal blanc* of the right great toe-nail, with recurring pustules and vesicles in this area for several months before lesions appeared on the dorsum of the left foot and on the elbow. In both cases reported by Barber and Eyre an injury to the finger-nail with resulting suppuration initiated the process. In both there was a typical dermatitis repens of the thumb, and in one there were moist crusted lesions on the palms and soles, associated with acute onychia. Christie and Anderson's [14] case followed a sliver beneath the thumb-nail and involved all the fingers, with a typical dermatitis repens.

The onset in the two cases reported here was different. There have never been any lesions about the hands or feet resembling acrodermatite

13. Darier, J.: Proc. Eighth Internat. Cong. Dermat., Copenhagen, 1930, p. 1198.

14. Christie, J. F., and Anderson, T. E.: Brit. J. Dermat. **43**:234, 1931.

continué or dermatitis repens. In case 2 the nails have never been involved; in case 1, only late in the disease, when the nail plates were distorted, separated distally and undermined by keratotic material and in places by accumulations of sterile pus.

The onset in case 1 was with a generalized redness and scaling that appeared in infancy, with prolonged recurrences in later childhood. Psoriasiform scaling patches appeared in the usual sites at the age of 15 years. In case 2, psoriasiform scaling appeared in the scalp at 8 years of age and on the trunk at 16 years.

During the periods of acute and subacute exacerbation, the two patients presented lesions that resembled closely the essential elements of acrodermatite continué. In the subacute stage, there appeared on the plaques minute ephemeral, flat-topped intra-epidermal lakes of pus which exfoliated in from twenty-four to thirty-six hours, only rapidly to reform. In the acute stage, these lakes of pus appeared generally on the reddened, edematous skin. During a major portion of the course, however, the plaques presented no such macroscopic elements, although histologically the micro-abscesses continued to reproduce. The plaques never presented an undermined margin with an up-turned collaret of scale, which was described by Hallopeau as characteristic of the disease. Audry emphasized the intractability and persistence of acrodermatite continué with the constant recurrence of pustules in the same area. In the cases reported here, there were no such permanent lesions. The lesions came and went without cause, and at times the patients were practically free from them.

The best histologic description of acrodermatite continué has been made by Kogoj,[15] from Pautrier's clinic; he described a typical case, confined to the hands for twenty-five years, in a man aged 69. This condition originated in the classic manner following an injury to the nail. The essential elements were subcorneal abscesses in the acanthotic epidermis which were filled with polymorphonuclear leukocytes. He compared the lesion to a sponge made up peripherally of small cavities which grow larger as a central cavity is approached. The peripheral cavities are unicellular vesicles; the larger ones, multicellular loculi. All are filled with polymorphonuclears, and the reticulum is made up of cytoplasm and cell membranes of cells which have resisted dissolution. Moderate papillary and subpapillary infiltration occurs, made up of connective tissue cells, lymphocytes and polymorphonuclears. There is marked emigration of polymorphonuclears through the epidermis. It must be acknowledged that this description is a fair reproduction of the histopathology found in the subacute stage in the two cases reported here.

15. Kogoj, F.: Acta dermat.-venereol. **8**:1, 1927.

PUSTULAR PSORIASIS

It is well known that the Munro-Sabouraud micro-abscesses in psoriasis may at times attain sufficient size to become macro-abscesses and appear as minute, flat, superficial pustules. In a case of chronic psoriasis of the ordinary type, which has been under observation in Dr. Ormsby's practice, such pinhead-sized, yellowish pustules appeared in a chronic plaque over the sacrum. It was impossible to obtain a biopsy specimen, but pus from these lesions was made up of polymorphonuclear cells in various stages of degeneration.

Von Zumbusch,[16] in 1910, reported as psoriasis with pustular exanthem two extraordinary cases occurring in a brother and sister. The first patient, a man, was observed over a period of twenty years, from 24 years of age to 44 years. He had suffered from psoriasis since childhood and always had a few plaques on the elbows and knees. During the twenty years he had been hospitalized nine times at the Riehl clinic in Vienna. The acute attacks were of sudden onset. At times they occurred apparently as the result of the application of antipsoriatic remedies for an exacerbation of the psoriasis, and at other times without apparent cause. The skin became erythematous, was scarlet over large areas, appeared tense and shiny, was edematous, dry and sensitive to the touch. The patient's temperature rose rapidly to 40 C. (104 F.), and he appeared very ill. In a short time, often within a few hours, minute superficial pustules filled with thin yellowish pus appeared on various areas of the skin. These multiplied rapidly until large areas were involved. The contents were sterile. Within a day or two the first pustules dried up, and the skin began to be covered with lamellated, moist crusts so that the pustules were no longer evident, the skin was dark red, and the crusts suppurated, leaving weeping surfaces. In the meantime new pustules formed at the margin. Erythema rapidly spread over the entire body. The patient appeared very ill and complained of persistent pain in the skin. This condition persisted a few days and sometimes longer. New pustules continued to appear in the same areas. Remissions of several days or weeks might occur between the crops of pustules. Finally, the fever fell, the redness faded, the patient felt well, and generalized scaling set in. In a few days the skin was dry, brownish red, somewhat infiltrated and covered with lamellated, dry scales. In other words, the patient now had an ordinary psoriasis. Unfortunately no histologic study was made in this case.

Schaefer[17] reported as psoriasis pustulosa a case from von Zumbusch's clinic in Munich, which, in its clinical and histologic findings,

16. von Zumbusch, L.: Arch. f. Dermat. u. Syph. **99**:335, 1910.
17. Schaefer, R.: Dermat. Ztschr. **33**:49, 1921.

resembled closely the two cases reported here. A man, aged 47, had suffered for nine years from recurrent plaques on the scalp, back and extremities. These consisted of coin-shaped plaques and were subject to periods of exacerbation, when they became edematous, inflamed and studded with transitory miliary pustules which exfoliated as thin crusts. During remissions these plaques were covered with psoriasiform scales. Microscopically, the characteristic miliary intra-epidermal abscesses were found beneath the stratum corneum and were exfoliated between the lamellae. There was marked acanthosis. The papillae approached very closely the surface. There was diffuse round cell infiltrate in the papillary and subpapillary layers of the corium, containing many polymorphonuclears. Case reports of pustular psoriasis are not uncommon in the German literature.

Barber [18] has extended the concept of pustular psoriasis to include not only disseminated pustular patches simulating acrodermatite continué of Hallopeau, a pustular phase in the transition of the ordinary psoriasis to exfoliative dermatitis, but also an unusual variety consisting of symmetrical groups of recurring pustules on the palms and soles resembling a fungus infection. He distinguished pustular psoriasis histologically by the presence of exaggerated micro-abscesses of Munro-Sabouraud in the upper rete, where the rete cells have been completely replaced by polymorphonuclears and mononuclears. According to his concept, it thus differs from the micro-abscess of acrodermatite continué of Hallopeau, which contains a reticulum of resistant malpighian cells forming the spongy structure of Kogoj and packed with polymorphonuclears. Clinically, he emphasized the fact that pustules of psoriasis always occur on pre-existing plaques or patches and never on the normal skin as they do in disseminated acrodermatite continué. He considered acrodermatite continué of Hallopeau an infection with staphylococcus.

While clinically my cases are a close duplicate of the cases of psoriasis with pustular exanthem reported by von Zumbusch and by Schaefer, it is a little more difficult at first sight to reconcile the histopathologic picture in the subacute and acute phases with the histologic picture to which one is accustomed in the static phases of ordinary psoriasis. Haslund [19] has made an unusually extensive study of all stages of psoriasis, and his findings are of great interest in connection with this identification. Haslund described the outward streaming of polymorphonuclears and serous exudate from the papillae to the surface as an intermittent process. In the same lesion areas of intense activity may be found side by side with areas of minimal activity. He emphasized

18. Barber, H. W.: Brit. J. Dermat. **42**:500, 1930.
19. Haslund, P.: Arch. f. Dermat. u. Syph. **114**:427, 1912.

the fact that the outpouring of serous exudate may be sufficient in force to separate some of the rete cells, compressing them and thus forming enlarged intercellular spaces. This intensity is usually reached only in early, acutely developed lesions and also at times in the center of old plaques. It is almost always associated with marked out-pouring of polymorphonuclear leukocytes, which fill the resultant intercellular spaces. He also noted that the intercellular edema may often cause vacuolar degeneration in the rete cells. While these accumulations of polymorphonuclear leukocytes are usually subcorneal, Haslund has published photomicrographs of sections taken from early active psoriatic papules which show micro-abscesses, spherical in shape and extending from the stratum corneum to the top of the underlying papillae. He also stated that the serous and cellular exudate may be so marked that the psoriatic papule is covered with a material that partakes more of the nature of a crust than that of a scale. Thus, one finds large intra-epidermal abscesses with reticular degeneration of the rete cells in their walls, a resistant reticulum and a crust scale, all described by Haslund as occurring at times in undoubted psoriatic papules.

After observing the two cases reported over a period of years, I have reached the conclusion that they are an unusual variety of psoriasis. My conclusion is based on the following facts:

(*A*) The clinical course. Periods of quiescence with a few psoriatic plaques in the usual locations are followed by subacute exacerbations during the late winter or early spring months and finally by periods of more intense activity. This is the usual course of many cases of psoriasis, except that it is exaggerated.

(*B*) The character of the lesions. In the interim phase these are flat-topped papules or level plaques covered with dry silvery scales. In the subacute phase they become more inflammatory. Small lakes of pus appear at the epidermis. These are ephemeral, and after twenty-four or thirty-six hours are exfoliated as scales. They are interpreted as Munro-Sabouraud marco-abscesses, which have attained a size visible to the naked eye. In the acute phase they are formed over large areas of inflamed skin. The pustules are sterile.

(*C*) The location of the lesions on the sites of predilection for psoriasis.

(*D*) Histopathologic picture of the lesions. The essential process is the continuous reproduction of micro-abscesses beneath the stratum corneum by the emigration of polymorphonuclears from the papillary vessels through the spaces between the edematous rete cells and the continuous exfoliation of their pyknotic nuclear contents between the lamellae of the parakeratotic stratum corneum. In the subacute phase

and the acute phase the inflammatory reaction is more marked than in ordinary psoriasis; that is, the edema is greater and the round cell infiltrate of the papillary and subpapillary layers is heavier, the emigration of leukocytes is increased, and edema of the rete results in reticular degeneration of the lymph spaces with accumulation of the polymorphonuclears in such quantity as to form macro-abscesses which are visible to the naked eye. These in turn are exfoliated in the same fashion as in the interim stage.

(*E*) Association in case 1 of an attack of acute polyarthritis followed by an acute exacerbation of the cutaneous trouble.

(*F*) Pustular manifestations. Similar instances of pustular manifestations of psoriasis have been described in the literature by von Zumbusch and by Schaefer.

SUMMARY

1. Two cases of an unusual psoriasiform eruption with recurrent pustular exacerbation have been described and studied histologically.

2. During the interim phase the lesions resembled ordinary psoriasis. During the subacute phase, which usually recurred in the late winter, the lesions became larger, more numerous and at times inflammatory. Intra-epidermic, ephemeral pustules appeared in the plaques. An acute phase sometimes followed the subacute phase, when the eruption became generalized and systemic symptoms appeared.

3. All attempts to demonstrate a causal organism have failed.

4. Tentatively, these cases are classified as pustular psoriasis.

DISCUSSION

DR. ISADOR ROSEN, New York: I am very much interested in this type of psoriasis and wonder whether Dr. Ebert has in the body of his paper something about the effect of treatment on these patients. I have had under observation two patients, both males, with lesions on the plantar surface of the feet; at first a diagnosis of dermatophytosis was made on account of the existence of vesicles in the substance of the lesion and also on the borders. After careful microscopic and cultural studies were made and found to be repeatedly negative this was ruled out. A final diagnosis of psoriasis was established by the appearance of characteristic lesions elsewhere. The plantar lesions were resistant to all forms of therapy. Did Dr. Ebert experience the same difficulty?

DR. FRED WISE, New York: I was much pleased to hear Dr. Ebert's paper dealing with a subject that has always been a controversial matter to me and to my confrères. The rarity of the disease is manifested by the fact that I have seen not more than one or two typical cases in twenty years. Rarely is a case presented at the meetings of the New York Dermatological Society.

I should like to know whether the articles written by Barber and Semon actually differentiate between this form of psoriasis and Hallopeau's disease, and whether this differentiation is made on the variable contents of the pustules. The case we had under observation for several years presented sterile pustules. The

name acrodermatite continué is justified, for the disease has a predilection for the toes and hands, clinically closely resembling dermatophytosis. I wish to emphasize what Dr. Ebert said about the constant finding of sterile pustules and also the marked resistance to treatment in these cases of pustular psoriasis. In a woman recently under our care, an astonishing number of therapeutic attacks were required to bring about even temporary removal of the pustular eruptions.

Dr. George M. MacKee, New York: I have never seen a case exactly like the one Dr. Ebert has just described. I am familiar with the exudative lesions of psoriasis, which must be differentiated from seborrheic dermatitis and dermatophytosis and also with lesions and eruptions that must be differentiated from syphilis and other diseases. I am familiar with the pustular type of psoriasis that is usually limited to the palms and soles and which must be differentiated from dermatophytosis and Hallopeau's acrodermatitis. Several of the speakers have mentioned vesicles occurring in this type of case. I have never seen vesicles occur. The elementary lesion is a pustule. This is important, and I think that it helps in the diagnosis between this condition and dermatophytosis.

I agree with the previous speakers as to the great resistance to treatment. The cases will not yield to the conventional treatment used in psoriasis. In my experience constant wet dressings have been the most effective measure.

Dr. Walter J. Highman, New York: The point of interest in this discussion, as Dr. Ebert so well indicated in his comments, is the fact that in inflammations of the skin we rarely find either a purely desquamating or a purely vesicular lesion. The two are invariably combined, the one dominating in what we are disposed to call scaling dermatoses and the other in vesicular dermatoses. In frankly vesicular dermatitis there is always a great element of scaling, and in the other type we can demonstrate vesiculation under the microscope. This particular type of dermatitis demonstrates the fact that the exudative type of the disease is similar to the abscess of Sabouraud-Munro. Whether that has anything to do with the resistance to treatment I do not know, but, according to my experience, it is difficult to get rid of psoriasis, of whatever type.

Dr. Hamilton Montgomery, Rochester, Minn.: I have recently reviewed the histopathology in sixty cases of psoriasis, including four cases of so-called pustular psoriasis limited to the palms and soles which showed all the histologic features portrayed in Dr. Ebert's cases. No micro-organisms could be demonstrated in the sections or in cultures in these cases. On the other hand, at the Mayo Clinic we had one case fulfilling all the requirements of acrodermatite continué of Hallopeau, in which positive cultures for cocci were obtained from the skin and in which the Gram stain of sections of the skin revealed collections of cocci within the epidermis. Until we know more about these two conditions, I believe we should endeavor to separate them on the basis of the foregoing criterion. I might add that our cases of pustular psoriasis limited to the palms and soles have been resistant to treatment.

Dr. Michael H. Ebert, Chicago: It is somewhat confusing to attempt to connect this type of case with that described by Barber. Barber described two cases that resembled somewhat the cases I have described, but he found staphylococci invariably present. He makes that a point of distinction between acrodermatite continué of Hallopeau and pustular psoriasis. Since the time of Hallopeau, later investigators have found the abscesses of acrodermatite continué to be sterile. The lesions start on the fingers and toes and later become generalized, always remaining sterile. I believe that my two cases are psoriasis and not acrodermatitis. Barber also described pustular psoriasis occurring on the palms and soles as ephemeral

pustules, recurring on the same areas and being extremely resistant to treatment. That is not the type of case that I have described. My case is the same type as that described by von Zumbusch and presented before the German Dermatological Societies. I said we had placed these cases tentatively in the psoriatic group. If we can find a casual organism, we may wish to change our minds, but I think that those who see the cases year in and year out will agree that they resemble psoriasis more than anything else. They do not resemble the acrodermatite continué of Hallopeau except in the acute stage, and then they revert to their resemblance to psoriasis.

DERMATITIS FROM THE OXYGENAIRE

REPORT OF A CASE

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Within recent years the list of substances capable of inducing an inflammation of the skin in sensitive persons has grown rapidly. Dermatologists everywhere have been on the alert to discover in the world of external contacts new causes of dermatitis.

The reaction of the skin to irritants of a chemical nature has long been a matter of interest. Some chemicals are harmless to most persons, but quickly provoke a dermatitis in isolated instances of individual susceptibility. There are many others which are strong enough to act as primary irritants, producing an inflammation on any skin.

Less importance attaches to the latter group save when the method of exposure is unusual. The case which I shall describe, though it involves a primary irritant, merits attention because of the singular circumstances surrounding the patient's contact with the chemical, and because of its practical implication.

REPORT OF CASE

H. M., a white man, aged 57, was admitted to the Memorial Hospital on Jan. 12, 1932, with a diagnosis of coronary thrombosis and chronic myocarditis. On January 25 he was having such respiratory difficulty as to necessitate placing him under the Oxygenaire, where he breathed a mixture of oxygen and carbon dioxide, the latter varying from 2 to 5 per cent. During the following nine days he had twenty-five seances with this machine, at irregular intervals, as needed, the exposures varying from thirty minutes to an hour.

Gradually a dermatitis developed, beginning on the face and spreading downward. When I saw him, several days after the last exposure, he presented an itching erythroderma, moist in certain areas, dry and scaling in others. In addition, the oral and nasal mucosae were inflamed and tender. The involvement was generalized *except that it stopped abruptly at the knees*, the legs and feet having been spared. This is readily understood when it is remembered that the proper adjustment of the oxygen tent and the bed clothing renders it difficult, or indeed impossible, for the gases to come in contact with these parts. The condition was subsiding under appropriate treatment when death supervened from cardiac failure.

COMMENT

It was obvious that the picture presented was due to the patient's seances with the Oxygenaire. That the oxygen or carbon dioxide gases per se could have been the source of irritation is, of course, incredible.

The only other possibility was the soda lime used to extract the exhaled carbon dioxide. This substance is placed in a compartment separated from the patient only by a wire screen. The mixture of air and oxygen passes through it into the tent under which the patient lies. So-called "soda lime" is a physical combination of sodium hydroxide and calcium hydroxide. No chemical reaction can occur between the two gases and these substances. The dermatitis must be explained, then, on the basis of a physical contact of the soda lime with the skin of the patient. It is easy to conceive how minute particles of this granular mixture could be caught up by the gas and wafted to the skin and accessible mucous membranes.

This opinion was concurred in by others, including the patentee of the Oxygenaire,[1] who stated that in his experiments with this machine he had seen irritation of the eyes and upper respiratory passages (though no dermatitis) produced by certain brands of soda lime, and that he had found another method of dealing with the exhaled carbon dioxide, as follows:

The oxygen output is turned to 8 liters or more, and the top shutter of the control box raised for five minutes. The increased flow of room air and oxygen entering the tent will drive the accumulated carbon dioxide out around the edge of the bottom of the tent. The lid is then closed and the oxygen reduced to the desired amount. Resort to this simple procedure eliminates the use of soda lime.[2]

SUMMARY

A case of generalized dermatitis slowly developing in a patient receiving daily exposures to the Oxygenaire is reported. Soda lime used to extract the exhaled carbon dioxide was incriminated as the cause. It was shown that the employment of soda lime is not necessary for the successful operation of this machine.

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1. Dr. T. A. Taylor, Lufkin, Texas.

2. Taylor, T. A.: A New Oxygen Therapy Apparatus, Texas State J. Med. **27**:436 (Oct.) 1931.

INFLUENCE OF GRENZ RAYS ON PATHOGENIC FUNGI IN SKIN MATERIAL

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Grenz rays are now widely used in the treatment of many dermatoses, including fungous diseases of the skin, for which the results obtained are usually even better than with x-rays. Since grenz rays are absorbed almost entirely by the superficial layer of the skin, just where fungi are found, it is logical to expect that such a type of radiation will influence fungous cells to a greater extent than more penetrative x-rays. Bucky [1] reported that of eighty-five cases of dermatophytosis in which grenz rays were used only 5 per cent showed a recurrence. In cases of tinea corporis also these rays proved effective, and in a few patients with tinea capitis the results in Bucky's experience were good even though epilation did not take place. Dorne and Cleveland White [2] treated fifty-two patients with superficial fungous infections of the skin with grenz rays and found that the infections due to yeastlike fungi, for instance, Monilia, responded uniformly to therapy, while those of hyphomycetic origin showed little if any improvement. The last quoted paper suggests the idea that the cure was due to the direct influence of grenz rays on fungi, and that the differences in sensitivity of various parasites to irradiation may determine the result of the therapy. Our experience in the clinic during the last four years (more than two hundred cases of tinea corporis and dermatophytosis) showed good clinical results in the majority of the cases in which grenz rays were used.

The understanding of the therapeutic effect of grenz rays in mycotic diseases of the skin requires obviously the study of their influence on pathogenic fungi under experimental conditions.

From the Department of Dermatology and Syphilology, New York University and Bellevue Hospital Medical College, service of Dr. Howard Fox.

1. Bucky, Gustav: Grenz Ray Therapy, translated by W. J. Highman, New York, The Macmillan Company, 1929.

2. Dorne, M., and White, Cleveland: Treatment of Superficial Fungous Infections with the Long Wave Length Roentgen Rays (Grenzrays), Radiology **18**:727 (April) 1932.

TECHNIC

In our practical medical work we deal with fungi not in the saprophytic state of pure cultures but in the parasitic state in the patient's skin. We deemed it therefore more interesting and nearer to natural conditions to experiment with fungi present in the skin rather than with pure cultures. To secure the largest possible amount of parasites and their most uniform distribution in the preparation, we used hairs affected by fungi from the scalp of children with tinea capitis. Several hairs taken from the patient's scalp were broken into small particles, mixed together and divided into two equal preparations, each preserved between two sterile slides wrapped in paper. One preparation served for the experiment, the other as a control. The technic of radiation was as follows: The preparation was unwrapped, and both slides were separated and exposed to the grenz rays in such a manner that the latter fell directly on the surface where particles of hairs were lying. We used for our experiments a grenz ray apparatus with Westinghouse tube with drawn-in thin glass window.

If the potential was 8 kilovolts, the tube current 8 milliamperes and the focal distance 5 cm., the tube produced a grenz ray beam of wavelength equivalent to half value layer of 0.012 mm. of aluminum. The dosage we used in the treatment of fungous diseases of the skin being from 500 to 800 roentgens, we started with the average therapeutic dose of 750 roentgens and then increased to enormous doses of 50,000 roentgens, which exceed many times the doses used in the therapy. The irradiated hairs were then planted in tubes with Sabouraud's medium. The control material from the same patient was cultivated under exactly the same conditions as to the medium, number and size and culture tubes and number of particles planted. The tubes were observed for several months, and the conclusion as to the viability of fungi was drawn from the fact of their growth on the medium.

Fungi tested that far belonged to the most common types of pathogenic hyphomycetes which affect the scalp in children, namely, Microsporon audouini, Microsporon lanosum, Trichophyton violaceum, Trichophyton crateriforme and Achorion schönleinii. We endeavored to take material containing the same species for subsequent experiments from different patients in order to diminish the rôle of individual variations in the resistance of fungous cells.

RESULTS

Twenty-two experiments were made with five different species of fungi taken from seventeen patients. The findings are summarized in the accompanying table.

Results in Twenty-Two Experiments *

	The Fungus				
Dose of Grenz Rays	Microsporon lanosum	Microsporon audouini	Trichophyton violaceum	Trichophyton crateriforme	Achorion schönleinii
750	−	..	−	..	±
7,500	+	..	+	..	+
30,000	+	..	+	..	+
50,000	+	+	0 ±	+	+

* + indicates normal growth; 0, no growth; ±, delayed growth; .., not tested.

Doses up to 50,000 roentgens did not influence these fungi: Microsporon lanosum, Microsporon audouini, Trichophyton crateriforme and

Achorion schönleinii. The results with Trichophyton violaceum were different. The doses up to 30,000 roentgens had no effect. However, 50,000 roentgens in two experiments completely inhibited the growth; the exposed hairs remained sterile while the control material gave numerous cultures. In the third experiment with the same species, only temporary inhibition was observed. Cultures from the exposed material started to grow later; they were at first smaller than the controls and only three months after planting reached the same size and development as the latter.

Besides the mere fact of growth or absence of growth, we also paid attention to the gross morphology of colonies, their tendency to pleomorphic degeneration and microscopic structure of mycelia and spores. No differences whatsoever could be found in cultures from irradiated material when compared with control cultures.

SUMMARY

1. Hairs containing pathogenic fungi were taken from children with tinea capitis, exposed to the grenz rays, and afterward the viability of fungi was tested by planting those hairs on a culture medium.

2. Grenz rays in doses up to 50,000 roentgens, therefore more than seventy times larger than the average single dose used in the treatment of fungous diseases of the skin, did not influence the growth of Microsporon audouini, Microsporon lanosum, Trichophyton crateriforme and Achorion schönleinii. The fungus Trichophyton violaceum was not affected by 30,000 roentgens. The dose of 50,000 roentgens completely inhibited its growth in two experiments and temporarily delayed it in the third one.

3. Fungous cultures which grew from the hairs irradiated by grenz rays did not show any peculiarities in their gross or microscopic morphology.

CONCLUSIONS

1. Pathogenic fungi in skin material are extremely resistant to grenz rays even in very large doses.

2. This resistance may differ in different species. Thus Trichophyton violaceum proved more sensitive to large doses of rays than some other species.

3. The therapeutic effect of grenz rays in fungous diseases of the skin is apparently due to the changed properties and reaction of the skin rather than to direct inhibitive influence of rays on fungi themselves.

SOME NONSPECIFIC DERMATOSES

THEIR RESPONSES TO SPLEEN EXTRACT

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In recent years the reticulo-endothelial system has been increasingly brought into discussions which sought to explain complex reactions within the body economy. Every branch of medicine and almost every abstruse subject in it have been coupled with this system. To the dermatologist, no less than to any other investigator, the reticulo-endothelial system has gained in importance at least in building several important theories. Thus there is evidence that the specific action of the arsphenamines is mediated through the reticulo-endothelial system; likewise the great postulated function of the skin as an immunity organ is related to this system, as is also the related subject of allergy. An important part of the reticulo-endothelial system, if only because of its mere bulk, is the spleen. This organ, which was so long a mystery to biologists and which has been cast in all sorts of rôles, has been recently used therapeutically in the form of its extract in several dermatologic entities. A few observers have reported their experiences with this extract, and some of their claims, if not extravagant, must be said to be remarkable and to furnish the dermatologist with a major weapon. In this communication I shall give a short account of my own investigations on the use of spleen extract in the clinic and in the laboratory.

The causes of nonspecific dermatologic conditions, such as eczema and dermatitis herpetiformis, remain obscure in spite of an immense amount of investigation. Many factors have been mentioned, but only a few merit serious consideration. What appears to be the single most important element—one which has been recently reemphasized—is the constitutional state of the patient. It has been said that persons so affected have an altered reactivity, a diathesis (Czerny). This state is a reflection of the total bodily metabolism. Diathesis and similar terms are vague ones which attempt to combine such specific factors as the activity of the endocrine glands, the organization of the nervous system, as shown in the autonomic nervous system balance, and the electrolytic and chemical make-up of the blood and lymph.

In order to gain a clearer notion of the measurable factors involved and their relation to and influence on one another my co-workers and I

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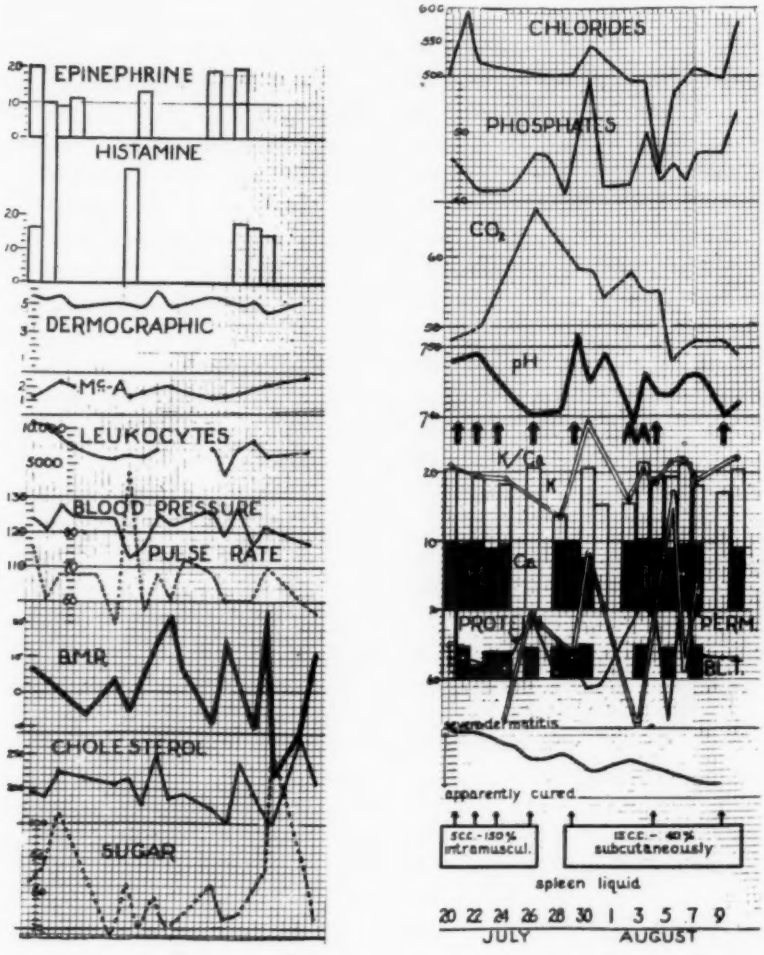
have carried on various estimations simultaneously from day to day for extended periods and correlated these estimations with the clinical condition of the patients. The same observations were also made later on the same patients while they were receiving spleen therapy.[1]



A *B*

Composite graph of data from a case of eczema. (The graph should be continuous, *A* above *B*, but was divided to facilitate printing.)

In order more closely to observe various changes taking place we studied two cases of dermatitis herpetiformis (Duhring's disease) and four cases of chronic eczema. These patients were admitted to the

1. The spleen preparation used was purified aqueous extract of hog spleen, supplied by the Wilson Laboratories, Chicago.

Research and Educational Hospital of the University of Illinois. They received a routine physical and laboratory examination and were followed for from one to three months. After a suitable control period they were placed on spleen therapy. In all, eighteen different observations were made every other day. These included: (1) capillary permeability (cantharides plaster method of Petersen); (2) serum protein (refractive index), calcium (the Clark-Collip modification of the Kramer-Tisdall method), potassium (Kramer-Tisdall), inorganic phosphorus (Fiske-Subbarow), p_H (Myers-Muntweiler) and carbon dioxide content (Van Slyke); (3) sugar (Folin-Wu), chlorides (Whitehorn) and cholesterol (modified method of Bloor) in whole blood; (4) basal metabolic rate; (5) pulse rate and blood pressure; (6) leukocyte count; (7) dermographic reaction time, and (8) McClure-Aldrich test and epinephrine and histamine flare.

In addition to these, observations were made on persons with dermatitis venenata whose exciting agents were used in patch tests before and during spleen therapy. The effect of spleen extract on the eosinophil count was investigated as well as the relationship of the clinical condition to the eosinophil count. Lastly, histologic studies were made to see what visible changes spleen extract might have on the inflammatory tissue.

RESULTS

Few changes which could be correlated with clinical improvement or relapse were observed, despite the numerous determinations. In dermatitis herpetiformis improvement was associated with: (1) an increased capillary permeability, the blister time being inconstant; (2) a lowering of the potassium calcium ratio; (3) a tendency toward acidosis, with a decrease in carbon dioxide content and p_H, both of these values, however, remaining well within normal limits; (4) a rise in the serum inorganic phosphorus, and (5) a lowering of the blood cholesterol.

In eczema still fewer correlations were observed. Improvement here seemed associated with an increased blister time, while the capillary permeability remained variable.

In both conditions what impressed me most, however, was the great variability and inconsistency of most of the reactions, while the clinical picture remained the same. This was especially manifest in the basal metabolic rate, blood pressure, pulse rate, blood sugar and chlorides, acid/base balance and flares.

Injections of spleen extract cause a decrease in the eosinophil count. This decrease comes on slowly, reaches its depth in twenty-four hours, stays down for about three days and then is followed by a rapid rise. The present results did not substantiate the report of Mayr and Mon-

corps,[2] that succeeding injections of spleen extract had more prolonged effects in reducing eosinophilia. The degree of depression in the eosinophilia ran somewhat parallel to the height of the eosinophilia. These changes in the eosinophil count could not be correlated with changes in the clinical condition sufficiently frequently in my opinion to indicate that these two were closely linked.

The observations with patch tests were made on three persons, sensitized individually to "Inecto" hair dye, lettuce and an unclassified garden weed, the ether extract of the last-mentioned substance being used. As a result of these observations the following conclusions were reached. When spleen extract is mixed with, or is allowed to wet, the material used for the patch test, the result of the test does not differ from that following the use of the same agents without spleen extract, nor can any influence be seen to follow the previous rubbing in of spleen extract at the site of the patch test. When spleen extract is injected locally into an area of dermatitis there follows an increase in the inflammation. I think that this increase is based merely on the nonspecific irritation caused by spleen extract (these injections are quite painful). There are no observable histologic changes in a dermatitis at any time during the three days following injections of spleen extract not given directly into the area of inflammation itself. When a patch test is made after the injection of spleen extract the intensity and the area of the inflammatory response are reduced. No change, however, in the elementary histologic changes is seen. The difference is merely quantitative.

Many dermatologists have been employing spleen extracts empirically to combat eczema. Almost all of them report favorable results. We, too, have succeeded in benefiting our patients by this method. The degree of improvement and the time in which this is achieved vary considerably. None of our patients was entirely relieved for a considerable length of time, and in most of them there was only partial amelioration. A sizable minority did not respond at all. We could not as a result of our investigations point to any invariable specific action of parenterally administered spleen extract. I do not think, however, that there is no specific action; on the contrary, the effects of spleen therapy do not entirely tally with those from the use of the usual nonspecific agents, such as foreign protein and preparations of some heavy metals.

In eight patients with urticaria I did not observe any clinical improvement which I could attribute to the use of spleen extract. While some of them showed improvement this could be accounted for on other grounds, such as the removal of septic teeth and a change in diet undertaken by the patient without my knowledge. In dermatitis herpetiformis two of four patients were apparently partially benefited, but after a

2. Mayr and Moncorps: Virchows Arch. f. path. Anat. **256**:19, 1925; **264**:774, 1927; München. med. Wchnschr. **73**:1777, 1926.

while relapse occurred in spite of the continued use of the extract. In eczema quite striking improvement followed the use of spleen in about 15 per cent of the cases. In none of these, however, was the improvement maintained. In one man who had come to the city from the country a relapse occurred shortly after he returned home. It is my belief that such spectacular improvements as were obtained could be accounted for by some factor other than the spleen extract if all the facts in each case were known.

COMMENT

The recent work of Petersen and his associates, stressing the importance of the peripherosplanchnic balance and the interrelationships of blood and tissues, is of fundamental importance. The periphery and skin and the splanchnic regions are constantly in balance, being oppositely oriented in respect to autonomic tonus. Similarly the blood and tissues are in constant chemical balance. In response to various stimuli this harmony may be upset, resulting in noticeable changes of bodily function and constitution. One of the most important of these changes is that which occurs in the capillary permeability. The arterioles of the skin have a certain sympathetic tonus which controls the rate of formation of the blister, while the capillaries themselves which are responsible for the degree of permeability are exposed chiefly to chemical stimuli and only indirectly to autonomic stimulation. In dermatitis herpetiformis, regardless of the initial degree of capillary permeability, the improvement is almost always associated with an increase. This is due largely to chemical influences, and associated with it there is a tendency toward acidosis and a lowering of the potassium/calcium ratio with an increase in inorganic phosphorus. These observations fit well together, since permeability increases in a more acid medium and as calcium leaves the cell. Usually the blister time increases with permeability, owing to a lowering of sympathetic arteriolar tonus, but here no constant effect is found. The blister time is variable. In eczema, on the other hand, the permeability is inconstant while the blister time becomes rapid. Here, then, as a result of therapy there is associated with improvement a decreased sympathetic tone of the peripheral arterioles.

What appears to be more important, however, and occurs even with clinical improvement is the marked instability of these patients both chemically and autonomically. The great fluctuations in the basal metabolic rate and other observations noted indicate a lack of ability to adjust rapidly to stimuli or an overcompensation for them. It may be that this state is responsible for the constitutional predisposition and is the underlying factor. This, too, elucidates the reason for the divergent results obtained by different investigators. One claims that the condition is due to acidosis, and another, to alkalosis; one says that the

calcium content is low, and another stresses the parasympathetic state. Whether the patient's condition is relatively acidotic or basic, sympathicotonic or vagotonic is of relatively little importance. No constant deficiency or overabundance of any factor is found, but rather a general instability.

But there may be objections that such a view of the background, while good enough in itself, neglects the more important specific element—a definite sensitizing substance evoking an altered or allergic response. Such a view, far from omitting the specific element, implies it. Let us assume the correctness of the modern conception of allergy based on partial digestion or conjugation of protein material by enzymes. Then overcompensated responses take the form of ready alterations of proteins to give products that are toxic, antigenic or so sluggish that digestion of the protein does not proceed fast enough to deprive it of antigenic capacities. In contrast, stabilized systems are not easily induced to manufacture products capable of sensitizing them, or they digest proteins rapidly to end-products that have no antigenic properties. They are thus not ready subjects for allergic processes.

It might be properly assumed that since persons with nonspecific dermatoses are exceptionally mobile as to some measurable factors, whatever improves them clinically should also tend to stabilize these unstable components. Such was not the case with spleen extract. Despite any improvements brought about by its use, no reflections of these were seen in terms of a stabilized background. It is my feeling, however, that the data presented here indicate but a part of the reactions responsible for the clinical changes and perhaps merely incidental to them.

SUMMARY AND CONCLUSIONS

Two patients with dermatitis herpetiformis and four with eczema were studied for from one to three months. Eighteen different observations were made every other day, before and during therapy.

1. The great general instability of the factors studied was the most outstanding observation.

2. This denotes an inability to adjust rapidly to stimuli or an overcompensation for them.

3. Such measurable instabilities are probably a few of the bases for such vague, inclusive terms as Czerny's diathetic state.

4. The capacity for allergy can be built from such a background.

5. In dermatitis herpetiformis clinical improvement was associated with: (*a*) increased capillary permeability; (*b*) an increase in the carbon dioxide content and p_H of the blood; (*c*) a decrease in the potassium/calcium ratio; (*d*) an increase in inorganic serum phosphorus, and (*e*) a decrease in blood cholesterol.

6. In chronic eczema the only correlation noticed was a shortening of the blister time, which indicates increased arteriolar sympathetic tone.

7. Injections of spleen extract cause a decrease in the eosinophil count which lasts for about three days.

8. This change in the number of eosinophils cannot be correlated with clinical changes.

9. Previous injections of spleen extract decrease the inflammatory response of a positive patch test.

10. There are no histologic changes in a dermatitis from the use of spleen extract.

11. At times spleen extracts are of distinct but limited value in eczema and other nonspecific dermatoses.

Dr. William F. Petersen helped in this study and provided laboratory facilities, and Dr. R. I. Klein aided in the preparation of some of the data.

THE USE OF EXTRACT OF SPLEEN IN CERTAIN DERMATOSES

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The use of extracts of spleen in the treatment of certain dermatoses has excited considerable interest since the work of von Zumbusch [1] and Mayr and Moncorps [2] abroad and of Paul [3] in America.

Von Zumbusch,[1] who utilized the observation of Ehrlich [4] that eosinophilia developed in splenectomized animals, was the first to call attention to the clinical relationship of defective function of the spleen to eosinophilia. Mayr and Moncorps [2] injected subcutaneously an albumin-free extract of hog's spleen into a group of patients who had itching dermatoses associated with eosinophilia, and reported diminution in eosinophils, decreased itching and general improvement. Schlack [5] also observed a decrease in the eosinophils of the blood after the injection of extract of spleen, but his results in the treatment of eczema with this preparation were not so striking as were those of the aforementioned writers. Subsequently, in a paper enthusiastically extolling the virtues of spleen therapy, Paul [3] reported excellent results in forty-four cases of eczema, in seventeen cases of urticaria and in other conditions. He used from 20 to 40 cc. of 40 per cent spleen extract.

Birke [6] used spleen substance in fifty-two patients with eczema associated with eosinophilia; he noted in all a decrease in eosinophilia, improvement in the condition of the skin in 93 per cent and complete recovery in 65 per cent of the patients. In another series of various dermatoses, such as scabies, pemphigus and arsenical dermatitis, he

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1. von Zumbusch, L.: The Question of Eczema and Exudative Diathesis, Urol. & Cutan. Rev. **31**:750, 1927.

2. Mayr, L. K., and Moncorps, C.: Eosinophilie und Milz, München. med. Wchnschr. **73**:1777, 1926.

3. Paul, T. M.: The Instantaneous Physiologic Cure of Eczema and Urticaria, Urol. & Cutan. Rev. **32**:452, 1928; **33**:724, 1929; **34**:380, 1930.

4. Ehrlich, quoted by von Zumbusch.[1]

5. Schlack, H.: Versuche unspezifischer Immunisierung durch Behandlung mit Extrakt aus Milzgewebe, Ztschr. f. Immunitätsforsch. u. exper. Therap. **57**: 499, 1928.

6. Birke, R.: Ueber Milzsafttherapie bei Dermatosen, München. med. Wchnschr. **75**:2009, 1928.

noted a decrease in eosinophils and itching, but no influence on the condition of the skin.

Sézary [7] reported good results in two cases of eczema, and Chevallier and Block [8] used 2 cc. of spleen extract (each cubic centimeter contained 12 grains [0.78 Gm.] of spleen substance), with good results in acute eczema and idiopathic pruritus.

Hadges [9] reported complete involution of an intractable diabetic pruritus after three weekly injections of extract of spleen, using 5 Gm. of spleen substance at each injection. Vallery-Radot and Blamoutier,[10] using 10 Gm. of spleen substance at each injection, reported six cures and two temporary improvements in ten cases of urticaria, and two cures and three favorable results in five cases of eczema.

MacKenna [11] reported six cases (three of urticaria, two of eczema and one of seborrheic dermatitis) in which he used only one injection of a 40 per cent solution of extract of spleen (15 cc.), with improvement only in the case of seborrheic dermatitis, which the author hesitates to attribute to the therapy.

Gaté and Charpy [12] used from 30 to 60 Gm. of fresh spleen substance at each injection in thirty-two patients (fifteen with eczema, twelve with prurigo, one with lichen planus, one with dermatitis herpetiformis, one with angioneurotic edema and two with psoriasis). They noted an immediate transitory decrease of the pruritus and diminution of the acuteness in the cases of eczema, with marked improvement only in the case of dermatitis herpetiformis and in two cases of eczema. All the other patients experienced a transitory amelioration of symptoms while under treatment.

Thus reports concerning the results obtained from the use of extract of spleen varied from the extremely enthusiastic ones of Paul [3] to the skeptical ones of MacKenna.[11]

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7. Sézary, A.: L'urticaire, Rev. crit. de path. et de thérap. **1**:49 (Feb.) 1930.

8. Chevallier, Paul, and Block, Leon: L'extrait aqueux de rate dans le traitement des prurits et des eczémas, Bull. et mém. Soc. méd. d. hôp. de Paris **54**: 1814, 1930.

9. Hadges, A.: Sur un cas de prurit diabétique irréductible guéri par l'extrait splénique, Arch. d. mal. de l'app. digestif **21**:107, 1931.

10. Vallery-Radot, P., and Blamoutier, P.: Essai de traitement de l'urticaire de l'oedéme de Quincke et de l'eczéma par un extrait splénique de porc. très concentré, Bull. et mém. Soc. méd. d. hôp. de Paris **54**:1666, 1930; Rev. prat. de biol. **23**:353, 1930.

11. MacKenna, R. M. B.: The Use of Extract of Hog Spleen in Dermatology, Lancet **1**:1401 (June 28) 1930.

12. Gaté, J., and Charpy, J.: L'action des extraits de rate sur les dermatoses prurigineuses, Bull. Soc. franç. de dermat. et syph. **38**:1222, 1931.

This report includes the clinical results in the use of spleen substances [13] during the past two years. Our interval of treatment varied from a day to a week, the frequency being determined by the clinical response. Patients who showed improvement within twenty-four hours after an injection were given subsequent treatments on alternate days, and the interval was lengthened as improvement progressed. In our more recent work, in which 500 per cent extract of spleen was used, a definite routine of 2 cc. daily given subcutaneously for seven injections, followed by injections on alternate days during the second week and two or three times weekly during the third and fourth weeks, depending on the completeness of clinical response, was instituted.

Differential blood counts and blood serum calcium determinations were made in some of the cases preceding, and again twelve hours after, the injections. Although we refer but briefly to a possible relationship between spleen therapy and calcium metabolism, there are numerous references in the literature indicating such an association. Our purpose in this paper, however, is to report on the clinical application of spleen substance in dermatology, so we merely mention this calcium-spleen association.

This series includes fifty cases. The patients in the first group included twenty-five patients who suffered with eczema; in thirteen the condition was chronic and of long duration and there was a history of eczema in infancy, asthma or hay fever. The patients ranged in age from a 7 month old infant, who had resistant acute infantile eczema involving the face, to a man, aged 70, who had chronic lichenified eczema of the face, neck, back and flexor surfaces of the arms of thirty years' duration. The only results noted in these patients with so-called "allergic" eczema was temporary relief from itching and, subsequently, diminution in the secondary traumatic dermatitis. In two patients (see the table) the cutaneous condition was aggravated while the patient received injections of spleen extract. When the spleen therapy was discontinued, however, improvement was noted following the use of local therapy, which had previously been ineffective. Contrary to Paul's [3] report, we did not notice any effect on an associated asthma or hay fever.

The second group of patients presented conditions such as seborrheic dermatitis, infectious eczematoid dermatitis, hypostatic eczema, various

13. Purified aqueous extract of hog spleen in the concentration of 150 to 500 per cent, respectively, supplied by the Wilson Laboratories, Chicago, was used in this work. The dosages represented by various percentages mentioned are as follows: 40 per cent spleen substance represents 0.4 Gm. of fresh hog spleen per cubic centimeter; 150 per cent spleen substance represents 1.5 Gm. of fresh hog spleen per cubic centimeter; 500 per cent spleen substance represents 5.0 Gm. of fresh hog spleen per cubic centimeter.

Table Showing Results of the Use of Extract of Spleen in Certain Dermatoses *

Name	Sex	Age	Diagnosis	Duration	Spleen Extract	Number of Injections	Eosinophils		Serum Calcium		Comment
							Before Treatment	After Treatment	Before Treatment	After Treatment	
G. F.	Male	7 mos.	Infantile eczema	7 mos.	5 cc.—40%	2	..	..	....	.....	No effect
E. D.	Female	14 yrs.	Allergic eczema	8 yrs.	5 cc.—150% 2 cc.—500% 2 cc.—500% 2 cc.—500% 15 cc.— 40%	3 3 1	3	4 3 2 1	9.97	10.29 10.66 8.46 10.45	Infantile eczema; temporary relief from itching; white cells, 14,250; blood pressure, 104 systolic and 58 diastolic; epinephrine, 7 minims; 20 minutes later; white cells, 25,400; blood pressure, 108 systolic and 58 diastolic
C. L.	Male	21 yrs.	Allergic eczema	5 yrs.	5 cc.—150% 15 cc.— 40%	4 2	21	13 10 8 8 20 12 16	....	.....	Infantile eczema; temporary relief from itching after injections
L. L.	Female	60 yrs.	Allergic eczema	20 yrs.	2 cc.—500%	12	6	..	....	.....	Condition aggravated; improved on local treatment
R. G.	Male	70 yrs.	Generalized eczema	30 yrs.	5 cc.—150%	2	3	2	8.62	9.81 9.67	Hay fever; no effect
C. H.	Male	21 yrs.	Seborrheic eczema of face and arms	2 yrs.	2 cc.—500%	11	..	..	....	.....	Decrease in itching; improvement in condition
I. S.	Female	49 yrs.	Infectious eczema, dermatitis of face and arms	5 yrs.	5 cc.—150%	15	13 7	7 5 6	10.14 10.56 9.15	9.81 8.81 9.33	Itching decreased temporarily after injections
B. S.	Male	66 yrs.	Hypostatic eczema	3 yrs.	2 cc.—500%	2	..	..	....	.....	Bland treatment; relieved when administration of spleen discontinued
E. N.	Male	35 yrs.	External irritant; dermatitis of face; toxic dermatitis of body	2 yrs. 1 yr.	15 cc.— 40%	5	4	1	....	.....	Marked improvement; involution in three weeks
G. A.	Male	37 yrs.	Pityriasis rosea; exfoliative dermatitis	.....	2 cc.—500%	10	..	..	....	.....	Improvement in exfoliative dermatitis; no effect on pityriasis rosea
J. B.	Male	33 yrs.	Postarsenical exfoliative dermatitis; had 12 injections of arsenic	2 mos.	2 cc.—500%	11	11	8	....	.....	Marked improvement at end of first week; complete involution at end of a month; still under treatment
M. D.	Male	.....	Acute urticaria; angioneurotic edema of face	4 days	10 cc.— 40% 5 cc.—150%	2	..	..	....	.....	Complete involution within four days
J. S.	Male	.....	Urticaria; angioneurotic edema	3 mos.	5 cc.—150%	6	..	..	....	.....	Marked improvement with cure in three weeks; slight recurrence five months later, with improvement on spleen therapy
A. G.	Male	49 yrs.	Chronic urticaria	9 yrs.	2 cc.—500%	5	..	..	....	.....	No urticarial lesions but itching persists
E. S.	Male	49 yrs.	Dermatitis herpetiformis	.....	2 cc.—500%	7	33	21	....	.....	Improvement in clinical appearance; decreased itching; feels well
T. V.	Male	22 yrs.	Pemphigus follaceus	3 yrs.	2 cc.—500%	7	..	..	....	.....	No change
A. M.	Female	32 yrs.	Lichen planus	2 yrs.	2 cc.—500%	3	..	..	....	.....	No change

forms of nondescript dermatitis of limited extent and of relatively short duration or secondary toxic exfoliative dermatitis. One of the patients in the latter group showed such a rapid response to spleen therapy that his case is worthy of special mention.

A Negro (G. A.), aged 37, when first seen, had a generalized maculopapular eruption on the trunk and extremities, which had the configuration of pityriasis rosea. He returned six days later, after using various proprietary ointments; there was a superimposed generalized exfoliative dermatitis. He appeared acutely ill and in great distress from pruritus and chilliness. He was hospitalized and given seven daily injections of 2 cc. of 500 per cent spleen extract; there was complete involution of the exfoliative dermatitis, and only the residual pityriasis rosea remained. Subsequent treatment during the second and third weeks did not affect the primary eruption.

Clinical improvement with decrease in acuteness, pruritus and infiltration was noted in the other cases in this group, but relapses occurred frequently after the treatment was discontinued.

The use of extract of spleen in postarsenical exfoliative dermatitis is being investigated further. The results obtained to date have been encouraging, but more work must be done before definite conclusions can be made.

Consistently good results were noted in a group of patients with urticaria. The clinical response that was obtained varied from complete cessation of itching, with the disappearance of the lesions, to only a diminution of the pruritus. These patients all had received previous treatment as a routine without appreciable benefit to the dermatoses. That improvement occurred from the spleen therapy itself may be inferred from the fact that remission occurred sooner under this treatment than could be accounted for by the self-limiting course of some of these diseases.

Favorable clinical response was observed in dermatitis herpetiformis. Four patients showed a marked cessation of itching with involution of the secondary traumatic dermatitis, diminution in the occurrence of the primary grouped lesions and marked improvement generally. No response was noted in two cases of pemphigus foliaceus, and there was no effect in one case of lichen planus.

The injections of extract of spleen are relatively harmless, except for pain of varying degree at the site of the injection. However, toxic reactions were noted in some of the patients. The reactions varied from a general sensation of warmth to fever, chills and general malaise coming on within a period of from twelve to eighteen hours after the injection and subsiding within twenty-four hours. In a girl, aged 18, with urticaria, profound shock developed after an intramuscular injection of 2 cc. of 500 per cent spleen extract, but she responded to an

injection of epinephrine. In another patient, temporary syncope of mild degree developed after a similar injection. The majority of patients, however, had no untoward effects.

Our incomplete observation on the blood serum calcium and eosinophils revealed inconstant results; there was a tendency, however, toward a slight increase in serum calcium and a diminution in eosinophils after the injection of spleen, with prompt return to the previous level within from twenty-four to thirty-six hours after treatment. Bayle,[14] Hale and Ablahadian [15] reported increased calcium and Nitschke [16] and Brougher [17] reported a decrease in serum calcium in their experimental observations on animals. Our observations confirmed those of Chevallier and Ely [18] that the effect on the eosinophils is only temporary, since the cause of the disease is not removed.

SUMMARY AND CONCLUSIONS

The results of our clinical experience with a purified aqueous extract of hog spleen indicate that it is of distinct value in urticaria, dermatitis herpetiformis and secondary toxic exfoliative dermatitis. Spleen extract has limited usefulness in the temporary alleviation of certain phases of the subjective sensations in eczema. It tends to decrease the pruritus and to shorten the period of acuity. It is of value as an adjunct to local therapy in resistant cases of dermatitis, or, as stated by Gaté and Charpy, it is an "addition to be used in stubborn disorders, especially for relief of itching." However, treatment must be prolonged, with a series of injections approximating 10 Gm. of spleen substance being given at each injection, over a period of time varying with the individual case. The more concentrated solution has the advantage of less fluid volume in each injection, but the disadvantage of more local pain and reaction. The spleen extract is relatively nontoxic. However, we were unable to substantiate Paul's "rapid findings of instantaneous cure" by the use of spleen extract.

104 South Michigan Avenue.
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14. Bayle: Therapeutische Mitteilungen, München. med. Wchnschr. **73**:351, 1926.

15. Hale, H. A., and Ablahadian, E.: The Function of the Spleen, California & West. Med. **23**:289, 1925.

16. Nitschke, A.: Darstellung einer den Calciumgehalt und einer den Phosphatgehalt des Serums senkenden Substanz, Ztschr. f. d. ges. exper. Med. **65**:651, 1929.

17. Brougher, J. C.: Effect of Desiccated Spleen and Splenectomy on Serum Calcium in Normal and Parathyroidectomized Dogs, Am. J. Physiol. **92**:648, 1930.

18. Chevallier, P., and Ely, Z.: Action de l'extrait aqueux de rate sur l'eosinophile sanguine, Bull. et mém. Soc. méd. d. hôp. de Paris **54**:1819, 1930.

FATALITY AFTER INTRAMUSCULAR INJECTION OF BISMUTH

IN A MAN SENSITIVE TO ARSENOBENZENES

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AND
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In a recent work entitled the "Treatment of Syphilis," we commented on the relative safety and harmlessness of bismuth compared with the arsenobenzenes and mercury. Furthermore, in clinic and office work we have given about 75,000 injections of bismuth without a single serious manifestation or symptom of intoxication. Beerman (*Arch. Dermat. & Syph.* **26**:797 [Nov.] 1932) recently reported 35 deaths due to bismuth in the treatment of syphilis, collected from the literature since 1922. To this number we add a death which we regard as unusual.

A man, aged 51, presented a florid secondary syphilis at the time of the first examination, and in accordance with our usual therapeutic policy, treatment was instituted with an intramuscular injection of 100 mg. of bismuth salicylate. During his examination he rested one hand on a table where neoarsphenamine had been mixed for a preceding patient and came in contact with a few drops of this solution which had been spilled. Within a few minutes he complained of a tingling sensation of this hand. During the next twenty-four hours there appeared an acute inflammatory dermatitis of the hand and wrist, and in view of this evidence of marked sensitization to the arsenobenzenes, therapy was continued with bismuth alone. The patient stated at this time that he had previously come in contact with neoarsphenamine in a physician's office with the same result, but had never had an injection of an arsenical. The bismuth therapy was well tolerated for fifteen successive injections given at three or four day intervals, although after the fifteenth the patient complained of feeling slightly ill for three or four hours. The symptoms were indefinite, and the patient regarded them as due to some other cause.

It was following the sixteenth injection of bismuth salicylate that death resulted. The technic was the customary one of inserting a 2 inch needle into the deep muscles of the upper part of the buttock, making a withdrawal tension on the piston of the syringe to be sure the needle was not in a vein, and then slowly injecting the bismuth. Within one minute the patient became somewhat cyanosed and loosened his collar and tie. A subcutaneous injection of 8 minims (0.5 cc.) of epinephrine was given immediately, but in spite of this the cyanosis increased, his eyes became congested, and the lips were swollen and bluish. He then lay down on the table and a minute or two later was in coma. A second injection of 8 minims of epinephrine was given. The patient's respiration became

increasingly difficult, and the pulse progressively weaker. When the pulse could no longer be felt, an intracardiac injection of 1 cc. of epinephrine was administered. There was no response to this. The patient died twenty-five minutes after receiving the injection of bismuth. At no time was there cough to suggest the possibility of embolism.

It was impossible to obtain permission for autopsy, but Beerman stated that postmortem data in two of the cases of sudden death collated by him were of no help in solving the cause.

The symptoms were uniform with those described by Beerman in deaths from acute conditions and regarded by him as manifestations of the symptom complex of colloidoclastic shock. In cases collated by him, the type of preparation and dose used, the type of syphilis and the sex of the patient seemed to be of no significance. In Beerman's series sudden death occurred chiefly after intravenous injection. The unusual feature in our case is the fact that the bismuth was injected intramuscularly.

We had come to regard bismuth as an eminently safe drug. This accident came to us, therefore, as a severe shock, as the death was unforeseeable and likewise unpreventable. We believe that the patient became hypersensitive to a bismuth protein which was formed immediately after injection.

TREATMENT OF SPIDER NEVUS

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As is well known, spider nevus consists of a central dilated capillary loop of the papillary layer of the skin, and from this radiate dilated capillaries, giving rise to its spider-like or starlike appearance. It is a harmless deformity, but frequently disfiguring, especially when it occurs on the tip of the nose. At times there is more than one central dilated capillary in the same red spot. I have seen three. They must all be treated to secure a perfect result.

The treatment consists in obliterating the central capillary. Sometimes this capillary is fairly distinct, sometimes not. Whether distinct or not, however, the diffusion of light by the superimposed epithelial layers, especially by the horny layer, always interferes with its being perfectly distinct. Furthermore, these layers intervene in any endeavor to introduce the electric needle, the hot point or the chemical employed to obliterate the central dilated capillary. Here again the horny layer constitutes the main interference.

As a consequence of these handicaps, failures in the treatment of spider nevi are exasperatingly frequent.

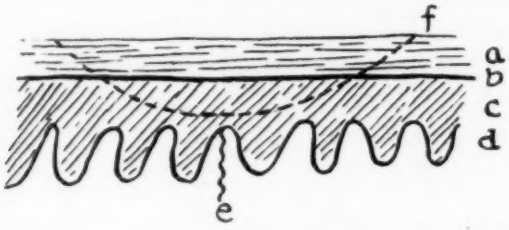
On reading the excellent article on "Grattage" in Desaux and Boutelier's recently issued manual of dermatology,[1] it struck me that the elimination of the upper epithelial layers there described would facilitate any procedure undertaken to obliterate the central dilated capillary. The elimination of these layers may be accomplished with a scalpel or curet, or better still, with a Dix corneal spud, as suggested by my associate, Dr. J. D. Viecelli. The instrument is held in the hand like a pen, and then, with repeated strokes given with a limber wrist, the layers of the epidermis are eroded off successively.

The procedure was first introduced by Louis Brocq for exploratory purposes, and he devised an excellent instrument for carrying it out, called an exploratory curet. It has a comparatively dull edge and is curved. It reminds me of a human finger-nail. On the roughened surfaces it is intended to explore it acts admirably, as the edges of the epithelial cells tend to curl up, and the instrument catches in these; the lightly repeated blows finally loosen the cells and carry them away. In spider nevus, however, the surface is frequently smooth, and it requires

1. Desaux, A.; Boutelier, A., and Brocq, P.: Manuel pratique de dermatologie, Paris, Masson & Cie., 1932, diagram 73.

a sharper instrument to get beneath the cells and to lift them off. Hence the previously mentioned spud, or a curet, is a better tool for this purpose.

In carrying out this procedure, first the scurf layer and then the horny and granular layer are eroded off down into the mucous layer. The operation is really a dissection of the layers of the skin. When the mucous layer is reached, there is a rich exudate of serum tinged with blood. If a pledget of cotton soaked in boric acid solution is allowed to remain on the eroded surface for a short time until the oozing ceases, the central vessel can be seen as a bright red dot. The boric acid solution must not be allowed to remain too long because, as an astringent, it will contract the vessels and the bright red dot will disappear. Also one must not give a preliminary injection of procaine-epinephrine hydro-



Cross-section of spider nevus. The corneous layer is indicated by *a;* the granular layer, by *b;* the mucous layer, by *c;* the papillary layer, by *d;* the central dilated capillary loop, by *e*, and the curve of erosion, by *f*.

chloride, as is so often done in minor surgical procedures, as this also would cause the blood vessels to contract.

The epidermis varies in its thickness in different persons, requiring a more shallow or a deeper erosion. Also, the walls of the blood vessels are more or less strong. If they are weak, a hemorrhage into the tissues may take place under the most carefully conducted erosion, and this purpura would obscure the field of operation.

As regards the choice of the means to obliterate the blood vessel, this may be done by electrolysis, or, as suggested by Toomey, with acid mercuric nitrate [2] or, as I prefer, with trichloracetic acid. A tiny piece of cotton is tightly wound on a wooden toothpick dipped into a saturated solution of this acid and bored down into the bright red dot.

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2. Toomey, Noxon: Principles and Practice of Dermatology, St. Louis, Lister Medical Press, 1930, vol. 3, p. 99.

TRICHOPHYTID OF THE HANDS

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The subject of the trichophytids has become so confused, as is evident after reading the article by Scholtz,[1] that it is time to formulate the knowledge and to point out which theories seem to be established and which are not.

There is a dermatitis of the feet, sometimes intertriginous, sometimes vesicular and sometimes scaly, occurring in both the acute and the chronic form, from which some type of mycotic fungus may so generally be recovered that it is reasonable to assume that the fungus is the etiologic factor. These are the cases ordinarily classified as tinea pedis. It is necessary to remember, however, that it is possible that similar lesions may be caused by other organisms.

A similar eruption occurs on the hands, and in a limited number of these cases mycotic organisms may be discovered. The proportion of cases of eruptions on the hands which yield mycotic organisms is, in my experience, very small. The cases in which a mycotic organism is demonstrated are to be classified as tinea manum.

Accompanying severe tinea of the feet, there is sometimes observed a transitory, follicular eruption on the trunk or elsewhere, corresponding in all particulars to trichophytid complicating kerion, as described by Jadassohn.

Accompanying severe tinea of other parts of the body, there has been observed, on the hands and feet, an acute, vesicular, transitory eruption. The vesicles are usually small and very superficial, and disappear after a few days without treatment. Mycotic organisms are occasionally, though rarely, found in these lesions in their earliest stages, but, as far as I am aware, never in the later stages. The sudden outbreak of this eruption, its transitory nature and the prevailing absence of organisms point to trichophytid as the most plausible explanation.

In severe cases of tinea pedis there sometimes appears, on the sides and dorsum of a foot from the sole of which mycelia have been recovered, an eruption of superficial vesicles, identical in appearance and in course with those described in the preceding paragraph; in these superficial vesicles I have never discovered mycelia. I believe that this eruption is a trichophytid.

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1. Scholtz, M.: Epidermophytids as a Clinical Conception, Arch. Dermat. & Syph. **25**:812 (May) 1932.

In the infections so far described, I have been dealing with an acute primary infection followed by a rapidly developing and transitory secondary eruption. I come now to debatable ground.

There is a small group of cases of eruptions of the hands and feet, the individual lesions of which are identical in appearance with those of tinea; that is, they begin as vesicles, usually small, and involute as a rule by absorption of the vesicular contents, leaving small brownish spots, which become scaly and fall, leaving reddened, scaly areas. There is seldom any exudation of serum on the surface, although this may occur. These cases differ from the ordinary cases in three particulars: 1. The extent of involvement of the sole or palm is very much greater. 2. They are exceedingly rebellious to treatment. 3. The discovery of the parasite is very difficult. I recall two cases seen at intervals—over a period of many months in one instance and of years in the other—and examined microscopically time and again. At only one examination in each case, and that early in my connection with it, was I able to find an organism. I do not know how to interpret these cases. They suggest the idea that in them the long duration of the infection has led to a profound alteration in the reaction of the skin, so that a minimum amount of organism or of toxin will produce a severe reaction, as occurs in a syphilitic gumma. As I have never been able to find the organism in the later stages of these cases, I can express no opinion as to its occurrence, but I incline to the belief that it occurs in very small numbers on both hands and feet.

There is a very large group of cases in which there has been tinea pedis for many years, sometimes active and sometimes so inconspicuous as to be overlooked by the patient. The hands of these patients are subject to the same eruptions that occur on other people. Among these eruptions is one which simulates very closely tinea pedis as seen on the hollow of the instep. There appear to be all grades between an acute outbreak of grouped vesicles and a dry, superficial scaling. In the vast majority of these cases, no mycotic organisms are found on the hands. These cases are essentially chronic, subject to exacerbations and remissions with or without treatment and hard to influence by local measures. They are also perplexing, and I know of no way of making a positive diagnosis. Very many of them appear to be caused by some external irritant, and I believe that in many of the cases the condition diagnosed as trichophytid or tinea of the hands, depending on the personal bias of the observer, has nothing to do with tinea. In other cases, however, I am led to suspect such a connection because of the clinical appearance, the sensitiveness of the patient to trichophytin and the fact that many such cases flare up following an exacerbation of tinea pedis. If, then, some of these chronic eruptions on the hands are connected with tinea, what is the relationship? The most simple explanation is that they are caused by local infection with the parasite. This explanation is not satis-

factory, because the most careful search fails to reveal the parasite in the vast majority of cases. If the parasite occurs at all, it must be in very small numbers. If the observer believes that the so-called "mosaic" is really a degenerate form of mycelia, he will of course report a large number of positive findings and will make proper evaluation of his results impossible. The alternative explanation is that the condition is trichophytid, for it is known by experiment that patients with trichophytid react differently to trichophytin than do normal people. But the eruption does not follow the course of trichophytid following kerion.

Kerion-trichophytid is acute and self-limited, and follows immediately an acute outbreak in the primary focus. Trichophytid complicating ordinary tinea pedis is chronic and rebellious to treatment and occurs usually, if not always, after a prolonged period of infection in the primary focus—often after this focus is forgotten. It seems as if a prolonged infection were necessary to produce the kind of sensitization necessary to this kind of response. The use of the same word to designate two such different conditions may seem contradictory, but there is a very close analogy in syphilis, in which the secondary lesions occur early and are transitory, while tertiary lesions appear late and are chronic, and present an entirely different clinical picture; yet both these are called syphilids. In late cases, the essential feature is the sensitization; organisms may occur in very small numbers, though I have not found them, even as they do in gummas, without invalidating the theory that an altered reaction of the skin is the basic etiologic factor.

The trichophytin test appears to be specific, and on careful examination of the patient and of his history, exceptions are usually found to be only apparent. Peck states (personal communication) that he has tested over fifty children between the ages of 6 months and 8 years, and that the test was positive in only one case, that of an 18 month old baby with fungus infection. But nobody claims that every eruption occurring in a patient with a positive trichophytin reaction is necessarily trichophytid.

It has been objected that all eruptions to which the name "trichophytid" was first applied occurred in patients with deep pyogenic, trichophytic lesions. This objection will not hold. Transitory lichenoid trichophytid has been repeatedly described in patients with superficial tinea capitis who had been treated with roentgen rays.

In conclusion, let me state my opinion that the diagnosis of tinea of the hands and trichophytid of the hands are both very much overworked. I believe that many cases so classed are dermatitis due to an external irritant, but that there remains a very small group of cases which are caused by a local infection with the parasite, and a larger group which is best explained as trichophytid.

"TOILET-SEAT DERMATITIS" PRODUCED BY A RED STAIN

POSSIBILITY OF A SUDAN STAIN AS CAUSATIVE FACTOR

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The location of a regional dermatitis often gives the clue which leads to the discovery of the cause. This is especially true when the eruption is limited to a relatively restricted area in the covered parts of the body, where the possibilities of contact with external irritants are not so numerous as with exposed portions, such as the hands and feet. In a consideration of dermatitis venenata, MacKee [1] stated that Fred Wise first called attention to a dermatitis occurring on the parts of the buttocks coming in contact with the toilet-seat, giving it the name "toilet-seat dermatitis." He believed that this condition might be due to varnish, lacquer, substances from hard woods, such as volatile oils, and excretions. Wise's observations are unpublished. MacKee described the case of a boy, aged 4 years, who presented an eruption consisting of erythema, slight infiltration and some scaliness and itching. It had been present for two years, improving at times but never disappearing. While irradiation improved the condition, it did not clear up until a porcelain toilet-seat was provided.

It seems that the following two cases are worthy of record in order to call wider attention to this clinical possibility, and because in one the stain employed in refinishing the seat was proved to be the causative factor.

REPORT OF CASES

CASE 1.—Mrs. E. F., American, white, 49 years old, who was referred to me by Dr. Richard Dexter, was seen first on Aug. 24, 1928. The eruption had been present since August 5. The lower part of the buttocks and the inner and posterior aspects of the thighs down to the knees were involved in a saddle-patch area. On the posterior portions of the upper part of the legs just below the flexures of the knee there were symmetrical patches the size of one's palms. The skin was intensely red and edematous and showed numerous large and small vesicles. No history of external irritants could be obtained. Ivy poisoning contracted on a summer excursion was suggested, but the patient denied any such possibility. Suspicion was next directed to the toilet-seat, but helpful information could not be secured from the patient, for her mind was preoccupied with her own theory of the dietary origin of the condition.

1. MacKee, G. M.: X-rays and Radium in the Treatment of Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1927, p. 498.

Instructions were given to protect the skin by covering the toilet-seat with paper, and simple local treatment was instituted. This consisted of potassium permanganate compresses and a calamine and zinc oxide lotion. About two weeks later, the patient returned, and after further questioning stated that two weeks before the condition began, her husband had refinished the toilet-seat with a red stain, following this with a coat of shellac and finally with varnish. She stated that occasionally she had violated my instructions about covering the toilet-seat with paper. While there had been marked improvement, there were still erythema and vesiculation in the saddle-patch area. Twelve days later the skin was practically clear. Specimens of the mahogany stain, the shellac and the varnish were brought by the patient. I applied portions to small and well separated areas on the anterior portion of the thighs. No change was visible in the skin at the end of an hour, but the next day there was an inflammatory reaction accompanied by marked itching at the point where the stain had been applied, while the other areas were normal.

CASE 2.—Mrs. C. D., an Italian, aged 52, was first seen at the dispensary of Charity Hospital on Jan. 28, 1929. For about five weeks she had had an eruption on the buttocks and on the upper part of the thighs. The entire area was erythematous, exudative and crusted. Inquiry elicited the fact that about six months previously the landlord had put a new red toilet-seat in her house.

A calamine lotion was prescribed, and the patient was directed to protect the skin by covering the toilet-seat with paper. A photograph was taken on January 31, when the condition had improved. On February 5 the condition was better but the eruption had extended below the knees. At several subsequent visits, there was improvement and then recurrence in areas, until the patient reported, on March 3, that the condition had cleared up entirely after a new white toilet-seat had been installed. She has been seen subsequently and has had no further trouble.

IRRITATING FACTOR IN STAIN

It was obviously impossible to trace the stain employed in the second instance, but the first patient was able to furnish the name of the brand. On inquiry, the manufacturers informed me that the dyes used in their stains were of the aniline oil and spirit-soluble type sometimes classed as sudan colors, also often called fat colors.

In examining the usual indexes to the medical literature, no reference was found to the sudan dyes as a cause of dermatitis, and they were not mentioned either in Weber's article [2] on external irritants or in Prosser White's [3] work on occupational dermatoses.

Merck's "Index [4]" lists the following stains of this group:

1. Sudan brown (pigment brown), fat-dye; alphanaphthalene-azo-alpha-naphthol.

2. Sudan red III, fat-dye; aminoazobenzenazo-beta-naphthol; tetraazobenzene-beta-naphthol. Used in coloring fats, spirit lacquers, etc.

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2. Weber, L.: A List of Cutaneous Irritants, Arch. Dermat. & Syph. **21**: 761, 1930.

3. White, R. Prosser: The Dermatergoses or Occupational Affections of the Skin, ed. 3, New York, Paul B. Hoeber, Inc., 1929, p. 383.

4. Merck's Index, ed. 4, Rahway, N. J., Merck & Company, 1930, p. 507.

3. Sudan yellow, Sudan I, anilineazobetanaphthol. Used in coloring spirit lacquers and oils.

4. Sudan yellow G, fat-dye; metadioxyazobenzene; anilineazoresorcinol. Used in coloring oils, varnishes, etc. Closely related chemically is scarlet red, which according to Conn [5] is a *di*-azo-naphthalene compound, similar to Sudan III, but differing in being a dimethyl derivative. It is also fat-soluble and is therefore a fat stain.

Solis-Cohen and Githens [6] refer to the power possessed by both sudan III and scarlet red of stimulating the growth of epithelium when injected into the skin or applied to granulating surfaces, but make no mention of local irritation. Sollmann,[7] however, stated that an ointment of scarlet red often produces irritation, even erosion, and sometimes even systemic effects. In spite of this, it is rather commonly used as a stimulating ointment.

Sudan III has been employed by physiologists for the study of fat metabolism. Mendel and Daniels [8] found that it was apparently nontoxic, as animals fed over long periods showed no deleterious effects. Read [9] administered sudan III dissolved in oil to animals intraperitoneally, subcutaneously and by mouth. The toxic effects occasionally encountered were attributed by him to the impurities contained in most commercial preparations.

It is regrettable that by the time I had ascertained the group to which the dye belonged the patient had disappeared from observation, and it was therefore impossible to determine whether this ingredient of the stain was responsible for the dermatitis. The spirit solvent is also a possibility, but did not impress me so strongly because of the probability of complete evaporation, due to its volatile nature, over such a period of time.

However, it seems desirable to report the data so that they may be available to other dermatologists when similar cases are encountered.

SUMMARY

1. In the two instances herewith reported severe dermatitis of the buttocks and posterior part of the thighs was shown to have been produced by red-stained toilet seats.

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5. Conn, H. J.: Biological Stains, ed. 2, Geneva, N. Y., Commission on Standardization of Biological Stains, 1929, p. 49.

6. Solis-Cohen, S., and Githens, T. S.: Pharmacotherapeutics, New York, D. Appleton and Company, 1928, p. 1013.

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8. Mendel, L. B., and Daniels, A. L.: The Behavior of Fat-Soluble Dyes and Stained Fat in the Animal Organism, J. Biol. Chem. **13**:71, 1912.

9. Read, B. E.: Behavior of Sudan III in the Animal Organism, J. Biol. Chem. **37**:121, 1919.

2. In one of the cases a red wood stain was proved by contact test to have been the source of irritation.

3. It was found that the wood stain contained a sudan dye, which was possibly the causative factor.

Editorial

TO JOSEPH JADASSOHN

In her inscrutable wisdom Providence has decreed that the "Magister Mundi Dermatologici" should suffer the loss of several of his greatest disciples. Schultz, Arndt and Lewandowsky have had untimely deaths, and now word has come that inexorable Fate has severed the thread of life of Bruno Bloch. We realize how great the grief these deaths are to one of the master's generous heart. In this hour of darkness the Editors extend their deep sympathy to Joseph Jadassohn, in the name of American dermatologists in general, and of his grateful American students in particular.

Correspondence

PIGMENTED EPITHELIOMAS

To the Editor:—The interesting article by Eller and Anderson, entitled "Basal Cell Epitheliomas with Excessive Pigment Formation," in the February issue of the ARCHIVES (**27**:277, 1933) contains points worthy of emphasis.

While basal cell carcinomas are not infrequent, they either are not recognized or are not deemed worthy of publication. One of the most interesting cases was published by Pautrier and Diss (*Bull. Soc. franç. de dermat. et syph.* **36**:498 [June] 1929). It was a sessile tumor of the scalp, showing the pseudocystic type of basal cell carcinoma, with large numbers of pigmented dendritic cells along the borders of some of the tumor masses.

Eller and Anderson quote H. Montgomery as stating that basal cell carcinomas with pigment are not rare, and Way is quoted as stating that he has rarely found pigment in the dermis in true basal cell carcinoma.

Failure to find pigment in carcinomas is undoubtedly due to the use of hematoxylin and eosin or similar stains, which mask the pigment. In connection with the preparation of a paper entitled "Melanotic Neoplasms of the Skin," I have studied 128 cases of carcinoma by means of the silver nitrate method, which enables one to see even a few granules of melanin pigment. The material included that of the clinic of the University of Chicago, and sections from the Clinique des Maladies Cutanées of Strasbourg, made available through the kindness of Professor Pautrier. There were 60 basal cell carcinomas, 14 carcinomas of intermediate type, 11 carcinomas of mixed type and 43 squamous cell carcinomas. There was pigment in 33 per cent of the basal cell carcinomas, in 14 per cent of those of intermediate type, in 9 per cent of those of mixed type and in 7 per cent of the squamous cell carcinomas. Five of the sections were from cases diagnosed clinically as pigmented basal cell carcinoma. It is thus seen that pigment is much more frequent than has previously been realized.

In considering the differential diagnosis, it is sometimes difficult to decide whether the case is one of pigmented basal cell carcinoma or one of melanoma, since the dendritic melanoblasts may be present in large numbers. The individual cells may be distinguished from those found in malignant melanomas by the fact that the granules are of normal size, are regular in size and are distributed regularly just within the periphery of the cell. In malignant melanomas the granules vary from barely perceptible, dustlike granules to large masses of melanin. This gives an irregular appearance which is striking.

Eller and Anderson's criticism of the term "melano-epithelioma of the skin" as suggested by Bloch results from the confusion of terms to which I have already called attention in an article entitled "Benign Epidermal Neoplasms" (ARCH. DERMAT. & SYPH. **26**:838 [Nov.] 1932). The condition described by Bloch as "non-nevoid melano-epithelioma" is not the basal cell carcinoma described by the authors. In fact, their figure 4, labeled "verrucous acanthotic nevus with pigmentation," is identical with case 2 of Bloch, and with a tumor that I have reported (Cutaneous Melanoma, ARCH. DERMAT. & SYPH. **21**:818 [May] 1930; figures 2 and 3). This condition is also similar to the benign epidermal neoplasms previously mentioned. If the term "epithelioma" were used in its logical sense to designate benign epidermal neoplasms of the skin and "carcinoma" used to designate malignant lesions, much confusion could be avoided.

S. W. BECKER, M.D., Chicago.

Book Reviews

Diseases of the Skin: A Manual for Students and Practitioners. By the late Robert W. MacKenna. Third edition. By Robert M. B. MacKenna. Price, $6. Pp. 506, with 45 colored plates and 149 illustrations. New York: William Wood & Company, 1933.

The third edition of "Diseases of the Skin" by Robert W. MacKenna, who died in 1930, has been prepared by his son Robert M. B. MacKenna. It retains all the characteristics of the original work, but has been revised and somewhat enlarged. Since the first publication of the work in 1923, it has taken its place among the good treatises on diseases of the skin which are especially for the student and the general practitioner. The third edition may be recommended, as have been the previous editions.

Die Hautkrankheiten, Leitfaden für Studierende und Ärzte. By Karl Herxheimer and Edmund Hofmann. Second edition. Price, 12 marks. Pp. 274. Berlin: S. Karger, 1933.

This edition of Herxheimer and Hofmann's "Introduction to Skin Diseases" is an excellent summary of the subject. Necessarily, the topics are considered briefly, but the essentials are emphasized. It is a good example of a difficult book to write, one that will give the student and the practitioner a satisfactory orientation of the important facts of the subject. The format of the work, the printing and the illustrations are excellent.

Obituary

BRUNO BLOCH
1878-1933

In the untimely death, on April 10, 1933, of Bruno Bloch, medical science has lost an active and energetic worker in the field of dermatology whose achievements brought honor to him, distinction to the two universities with which he was successively connected and credit to the special branch of medicine which he represented.

Born on Jan. 19, 1878, in the hamlet of Endingen, Kanton Aargau, Switzerland, Bloch, after completing the customary medical training, was appointed "privatdocent" in 1908, and "professor extraordinarius" in 1913, by the University of Basel. In 1916, he accepted a call to the University of Zurich as "professor ordinarius."

In both universities, Bloch was the first incumbent of the newly created chair of dermatology and venereology, subjects which previously had been taught by the professor of internal medicine.

Although Bloch had the benefit of the sage counsel and long experience of Jadassohn in the organization of the new departments, it nevertheless consumed much time and energy. In spite of these administrative duties, a series of publications recording the results of extensive and intensive research continued to appear from his pen. Whereas in Basel Bloch was handicapped by cramped quarters and inadequate facilities, Zurich provided him with a clinic and a research institute which were the envy of his colleagues and which, thanks to Bloch's growing reputation, soon became the Mecca for dermatologic research workers.

Among his contributions, reference may be made to his studies entitled "General and Experimental Biology of the Dermatomycoses Due to Hyphomycetes," "The Skin and Metabolism," "The Pigment of the Skin," "The Artificial Production of Metastasizing Carcinomas in Mice by Constituents of Coaltar," "The Experimental Production of Röntgen-Carcinomas in Rabbits" and "The Pathogenesis of Eczema." These titles show, perhaps meagerly, the spheres which he touched with the hand of a brilliant, pathfinding leader.

Bloch did not confine himself to research work. He functioned as director of the university clinics for dermatology and venereal diseases and gave the prescribed courses in these branches of medicine to the medical students. For a time he was president of the Swiss Association Against Venereal Diseases and issued a publication on this subject.

Bloch also was one of the co-editors of the *Archiv für Dermatologie und Syphilologie* and of the *Dermatologische Zeitschrift,* and one of the collaborators and contributors to Jadassohn's "Handbuch der Haut-und Geschlechtskrankheiten."

Such, briefly, is a partial outline of the professional activities of this man whose life was devoted to the study of dermatologic problems, a field in which his pioneering investigations earned for him a well merited international recognition as one of the forceful propagators of the concept of "dynamic" dermatology.

What he achieved will stand, in the years to come, as an impressive record of his indefatigable industry, of his executive talents for organization, of his skill in the selection of the co-workers for his researches, of his originality and technical ability in bringing investigations to fruitful termination and of his keen powers of discernment in the interpretation of experimental findings. His death is a major loss to dermatology.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE BIOLOGIC RELATIONSHIP BETWEEN COW'S, GOAT'S AND HUMAN CASEIN. A. F. ANDERSON, O. M. SCHLOSS and H. C. STUART, Am. J. Dis. Child. **44**:1178 (Dec.) 1932.

1. Experiments in active sensitization revealed that cow's, human and goat's caseins sensitize against each other.

2. Serums prepared against cow's casein gave positive precipitin reactions to human casein, and serums prepared against human casein reacted positively with solutions of cow's casein.

3. Animals that were passively sensitized to cow's casein exhibited evidences of anaphylaxis when given human casein intravenously. The converse was equally true.

4. The results seem to indicate a close biologic relationship between cow's, human and goat's caseins. It is possible that this similarity may explain difficulties that are encountered in the treatment of allergic states by the substitution of one milk for another.

AUTHORS' SUMMARY.

SOY BEAN (VEGETABLE) MILK IN INFANT FEEDING. F. R. RITTINGER and L. H. DEMBO, Am. J. Dis. Child. **44**:1211 (Dec.) 1932.

The author reports the results of a preliminary study of the feeding of soy bean (vegetable) milk to fifty infants over a period of a year. While the paper is concerned mostly with matters of interest to the pediatrician, it contains much information as to the composition of soy bean milk in regard to fats, carbohydrates, proteins, vitamins and ash, which is valuable to dermatologists who prescribe soy bean milk for infants sensitive to cow's milk.

DISTURBANCES OF FUNCTION OF THE SUPRARENAL GLANDS IN CHILDREN. H. J. FREEDMAN, Am. J. Dis. Child. **44**:1285 (Dec.) 1932.

An infant had hyperpigmentation of the skin on the face and on the back of the left leg and buttock. There were also hair on both cheeks, fuzz on the upper lip and generalized fuzz on the body, with a moderate amount of hair on the back and the vulva. Menstruation occurred monthly for four months. Symptoms pointed to involvement of the suprarenal cortex.

RESULTS OBTAINED FROM THE USE OF VARIOUS TUBERCULIN TESTS. E. FRIEDMAN, M. H. BLACK and A. L. ESSERMAN, Am. J. Dis. Child. **45**:58 (Jan.) 1933.

A comparative study of the various diagnostic cutaneous tests with tuberculin demonstrated the utter unreliability of the Pirquet (cutaneous scratch) and the modified Moro (inunction) test. The superiority of the Mantoux (intracutaneous) and "single puncture" methods was shown.

THE ARTHUS PHENOMENON: A SEROLOGIC STUDY IN A SYPHILITIC CHILD WITH A FATAL REACTION TO TRANSFUSION. I. H. TUMPEER and E. J. COPE, Am. J. Dis. Child. **45**:343 (Feb.) 1932.

A severe gangrenous lesion of the buttock followed the injection of diphtheria antitoxin into a patient who was still manifesting signs of reaction from a previous dose. This patient four years previously had received three immunizing injections

of horse serum toxin-antitoxin. Such a combination of events is termed the Arthus phenomenon; it corresponds to serum anaphylaxis in animals. The patient died following a transfusion. Experimentally a reaction typified as necrosis was produced by the interaction between the patient's and the donor's serum. It was shown that the fatal reaction to transfusion, despite compatibility of the agglutinins and hemolysins, was due to other changes in the patient's blood incident to the Arthus phenomenon. Reactions of this type may be looked for more commonly now, when the many children immunized during the last decade with horse serum toxin-antitoxin come in contact with other types of horse serum.

ANDERSON, Los Angeles.

AN INVESTIGATION OF SPIROCHETOSIS OF THE DENTAL ANLAGE IN CONGENITAL SYPHILIS. THOMAS J. HILL, Am. J. Path. **7**:515 (Sept.) 1931.

The enamel organ of the central incisor and first molar of the permanent teeth was examined by various spirochete stains. Despite the demonstration of spirochetes in six livers from cases of congenital syphilis, it was impossible to find them in the dental anlage. Therefore, it is concluded that the characteristic congenital syphilitic dental deformities are not the direct result of the invasion of the enamel organ by Spirochaeta pallida.

MOORE, Charlotte, N. C. [AM. J. DIS. CHILD.]

MELANOMA STUDIES: II. A SIMPLE TECHNIQUE FOR THE DOPA REACTION. GEORGE F. LAIDLAW and SOLON N. BLACKBERG, Am. J. Path. **8**:491, 1932.

The authors describe a simple technic for Bloch's dioxyphenylalanine (dopa) reaction. Three stock solutions are prepared and kept in the refrigerator: (*a*) a 1:1,000 solution of 3, 4-dioxyphenylalanine in distilled water; (*b*) 11 Gm. of disodium hydrogen phosphate in 1,000 cc. of distilled water, and (*c*) 9 Gm. of potassium dihydrogen phosphate in 1,000 cc. of distilled water. The reagent must be slightly alkaline. Just before the sections are cut, the reagent is buffered by adding 6 cc. of the sodium phosphate and 2 cc. of the potassium phosphate solution to 25 cc. of the dioxyphenylalanine solution, giving the optimum p_H of from 7.3 to 7.4. Frozen sections of fresh tissue are immersed in 5 or 10 cc. of the mixture at 37 C. for from four to six hours. After two hours and every hour thereafter a section is examined microscopically. Melanoblasts and myelogenous leukocytes blacken slowly; the rest of the tissue remains colorless. When the melanoblasts are stained sufficiently, the sections are rinsed in distilled water, dehydrated, cleared and mounted in balsam by any of the usual methods.

The reaction may be hastened either by using a higher temperature, from 58 to 80 C., or by increasing the alkalinity to 8 or even higher. Such reactions are finished in an hour or two. Rapid reactions should be controlled with the microscope every twenty minutes, for the fluid blackens quickly from the accumulation of dioxyphenylalanine-melanin and the sections are likely to overstain. Slow reactions give the more delicate pictures.

The tissue must be fresh. After death or excision from the living body, the reacting ferment diffuses quickly into the surrounding tissue and disappears. Fixation in a dilute solution of formaldehyde, U. S. P. (1:5) for not longer than three hours is permissible and facilitates the cutting of frozen sections. Other fixatives destroy the ferment quickly. No successful way has yet been found to preserve the tissue for a longer time than a few hours. However, after the reaction has taken place, the stain is permanent. Before staining, neither the block of tissue nor the sections should be permitted to lie in water for longer than the few seconds of a quick rinse, for water extracts the ferment quickly. The sections are dropped from the microtome knife directly into the freshly prepared dioxyphenylalanine mixture.

An important innovation introduced by the authors is the renewal of the mixture at the end of half an hour and several times thereafter if the fluid darkens before the melanoblasts are fully stained. Renewal of the reagent extracts from the tissues any excess of acid or alkali that would interfere with the reaction and by removing the accumulated dioxyphenylalanine-melanin prevents the common fault of overstaining.

Contrary to the opinion of European workers, the authors find that surgical preparation of the skin with iodine does not interfere with the reaction. They find it to be a specific stain for melanoblasts and for myelogenous leukocytes. Bloch's special technic for leukocytes is described.

LAIDLAW, New York. [ARCH. PATH.]

A CONDITION SUPERFICIALLY RESEMBLING MOSSY FOOT, IN A NATIVE OF SUDAN. N. L. CORKILL and D. SCANDER, Ann. Trop. Med. **26**:267 (Oct. 29) 1932.

In the case reported the foot was greatly enlarged and exhibited various-sized bosses on the dorsum. A papillomatous growth was present on the dorsum, on the sides and on other areas of the foot which did not come in contact with the ground. The papillae of this growth were as much as 5 mm. in length, dry, horny and slightly tender, but they did not bleed when avulsed. Tactile sensation was diminished in the papillomatous areas, but sensation to pain was increased. On the anterior surface of the lower third of the leg was an ulcer of thirty years' duration.

On section, a solid, opaque, whitish-gray layer, about an inch (2 cm.) thick, was found between the epithelial layers and the deeper tissues; this layer did not, however, infiltrate the muscles or fascia. It was firm and fibrous and contained some blood vessels, but otherwise had no definite macroscopic structure.

Stains of sections showed no organisms. No etiologic clue was established except that the process seemed to be granulomatous, with excessive deposit of fibrous tissue.

The condition differed from mycetoma in that there were no sinuses, granules or involvement of bones or tendons, and no fungus was cultured.

YAWS AND SYPHILIS. B. D. BLACKLOCK, Ann. Trop. Med. **26**:423 (Oct. 29) 1932.

Blacklock makes a careful and complete analysis of the arguments advanced for the separate entity of frambesia and syphilis. He believes, however, that the two conditions are the same, but that the process of frambesia is modified by age, race and local conditions.

He states that: (1) Frambesia is not transmitted in utero as syphilis is in many instances; (2) the primary lesion of frambesia is extragenital while the syphilitic chancre is usually genital; (3) syphilis seldom imitates frambesia; (4) mucous membranes are affected in syphilis but not in frambesia; (5) itching is common in frambesia but rare in syphilis; (6) alopecia is unknown in frambesia but may occur in syphilis; (7) this may also be said of ocular disturbances, iritis being observed often in syphilis; (8) in frambesia no visceral lesions are present nor is the nervous system seriously affected, in contradistinction to the findings in syphilis; (9) frambesia presents no endothelial proliferation while endarteritis obliterans is often found in syphilis, and (10) frambesia produces slight constitutional symptoms and does not respond well to treatment with mercury as does syphilis.

AN EXPERIMENT FOR IMMUNIZATION AGAINST CUTANEOUS LEISHMANIASIS. V. K. DI LOTTI, Ann. Trop. Med. **26**:545 (Dec. 16) 1932.

By the method of passive immunization, a small cutaneous graft was transplanted from an immune person to an incision in the skin of the person to be immunized. In one group of cases, the skin was removed, from an intact area in the vicinity of a scar from oriental sore contracted from one to six years before.

In twelve cases in Bagdad, four patients remained well and three contracted cutaneous leishmaniasis.

In a second group, the disease had been contracted from twenty-nine to forty years before, and the attempt at immunization was a failure.

No other means of immunization is effective, and the method described may be of use in protecting the children of Europeans in endemic centers.

STUDIES IN CHEMOTHERAPY: IX. SODIUM THIOSULPHATE AND ARSENIC RESISTANCE. W. YORKE, F. MURGATROYD and F. HAWKING, Ann. Trop. Med. **26**:587 (Dec. 16) 1932.

In a series of experimental attempts to support Citron's contention that sodium thiosulphate can destroy the resistance of arsphenamine-fast spirochetes, the authors were unable to influence the resistance of Trypanosoma rhodesiense which was sodium arsanilate-fast and neoarsphenamine-fast.

Sodium thiosulphate was given to infected mice, and the organism was exposed in vitro to sodium thiosulphate, but no effect on the resistance to arsenic was noted.

JAMIESON, Detroit.

STUDIES IN EXPERIMENTAL SYPHILIS: X. OBSERVATION ON CROSS-INOCULATIONS WITH HETEROLOGOUS STRAINS OF SYPHILITIC VIRUS. A. M. CHESNEY, T. B. TURNER and F. H. GRAUER, Bull. Johns Hopkins Hosp. **52**:131 (Feb.) 1933.

The facts brought out by the experiments reported by the authors and by their study of a large group of patients with syphilis furnish additional support for the view advanced by Kolle that immunity to syphilis in rabbits is limited to homologous strains of the syphilitic virus, but in man may be effective against other strains as well.

THE ABILITY OF PATIENTS TO PAY FOR THE TREATMENT OF SYPHILIS. M. M. DAVIS, J. Social Hyg. **18**:378 (Oct.) 1932.

Taking into consideration the average incomes of employed persons, Davis shows that for over 80 per cent of the population, the minimum cost of treatment of syphilis at minimum private rates would amount to more than 10 per cent of their annual incomes. He draws the following conclusions:

1. About 80 per cent of the population cannot pay for adequate treatment of syphilis at private rates.

2. About 50 per cent of the population can pay for treatment at pay clinic, rates, although not at private rates, except when the usual minimum fee is cut to about half.

3. Fully one third of the population, if infected, must receive treatment for syphilis free or for nominal amounts.

4. The cost of treatment for syphilis is an important cause of the insufficient or inadequate treatment which many infected persons receive.

ANDERSON, Los Angeles.

ARGYRIA: REPORT OF A CASE IN A PATIENT AGED FIVE AND A HALF YEARS. LAWRENCE T. ROYSTER, J. Pediat. **1**:736 (Dec.) 1932.

Argyria developed as a result of repeated irrigation of the nose with neosilvol solution. A functional heart murmur along with blueness of the skin had led previously to an erroneous diagnosis of heart trouble. Sections obtained by biopsy showed brown pigment in and around the basal layer of the sweat glands.

VON RECKLINGHAUSEN'S DISEASE IN CHILDREN: REPORT OF A CASE PRESENTING PIGMENTATION AND BONE CHANGES. SIDNEY D. LEADER and MILTON J. H. GRAND, J. Pediat. **1**:754 (Dec.) 1932.

A case of Recklinghausen's disease in an 11 year old American boy is reported. Brown patches had been present on the skin since birth. The bones appeared normal in the roentgenograms, except for a region of decreased density on the medial aspect of the distal end of the left femur. There were no subcutaneous nodules. Intelligence was unimpaired. No family history of the disease could be elicited. Similar cases of Recklinghausen's disease reported in the literature are discussed. LE MASTER, Evanston, Ill. [AM. J. DIS. CHILD.]

NEW ENGLAND HEART ASSOCIATION. OBSERVATIONS UPON CARDIOVASCULAR SYPHILIS. TRACY B. MALLORY, New England J. Med. **208**:177 (Jan. 26) 1933.

Syphilis involves the cardiovascular system most often in the aorta, the part affected determining the effect on the heart. In eighty autopsies in cases of syphilitic aortitis, aortic regurgitation was found in 27.5 per cent. Aortic stenosis was not found. The fact that the syphilitic process begins as an obliterative endarteritis of the vasa vasorum and causes a fibrosis in the valve leads to regurgitation as an end-result rather than stenosis. The author doubts that the dilatation of the aortic ring commonly found in syphilitic heart disease is specific; he believes it an evidence of generalized cardiac dilatation. In this group only fifteen patients showed narrowing of the mouth of one or both coronary arteries. All but one of these were in the group with definite involvement of the valve. Aortic regurgitation seems to be an essential manifestation of syphilitic involvement of the coronaries.

THE DIAGNOSIS OF CARDIOVASCULAR SYPHILIS. PAUL D. WHITE, New England J. Med. **208**:179 (Jan. 26) 1933.

White made a careful study of seventy-eight clinical cases seen in private practice, and also of fifty cases in which autopsy was performed. The seventy-eight clinical cases constituted only 2.4 per cent of the cases of organic heart disease seen in private practice. There were sixty-six males among the clinical patients, and forty-two in the group examined post mortem. Fifty-one per cent of the patients were between 50 and 60 years old, and 24 per cent were between 40 and 50. An unusual case of congenital syphilis was included. Cardiovascular syphilis is commoner in Negroes and less frequent among Jews. In the clinical group twenty-three had anginal symptoms, and eighteen, cardiac asthma. Conversely, cardiovascular syphilis was found in only 6 per cent of five hundred cases of angina, and in only 12 per cent of two hundred and fifty cases of cardiac asthma. Free aortic regurgitation was the most common sign found in the cases accompanied by cardiac enlargement. Roentgenologic studies are necessary, but the results are often misleading unless interpreted with great care. Hypertension and congestive failure are not characteristic. Syphilis of the central nervous system was found in about 30 per cent of the cases in which autopsy was performed. Seventy-eight per cent of the patients gave positive Wassermann or Hinton tests.

THE TREATMENT OF SYPHILITIC CARDIOVASCULAR DISEASE. C. MORTON SMITH, New England J. Med. **208**:185 (Jan. 26) 1933.

Prompt recognition of all syphilitic infections and adequate treatment are emphasized as preventive measures. Due allowance for the age, and especially the general physical condition, of a patient, must be made. Potassium iodide is necessary in practically all cases. Mercury or bismuth should be used before arsphenamine is employed, and in general in small doses and over a longer period. Bismarsen has been very useful. The use of other drugs, rest and occupational therapy is also discussed.

[Levine, in discussing the three preceding papers, emphasized as of diagnostic importance an aneurysm of the aorta, aortic insufficiency, a positive Wassermann test, a past history of syphilis and other stigmas of the disease. In 10 per cent of the cases of syphilitic aortitis these may be lacking. In cases in which congestive heart failure is present antisyphilitic treatment does not help, and may be harmful. It is best to use the same methods of treatment used in nonsyphilitic cases, and later employ antisyphilitic treatment, using arsphenamine with great care.]

PERSISTENTLY POSITIVE BLOOD REACTIONS IN TREATED SYPHILIS. WILLIAM D. WHEELER, New England J. Med. **208**:319 (Feb. 9) 1933.

Two hundred patients whose serum persistently gave positive reactions were studied. This group represent two thirds of the number found in the 1,200 patients under treatment during a year. Careful medical examination showed that 192 had definite syphilitic involvement of one or more organs; 65, cardiovascular lesions; 24, neurosyphilis, and 22, splenohepatic lesions. Barely 5 per cent had no symptoms. In 147 cases treatment was started from two to forty years after infection. All the patients persistently gave positive Hinton reactions; 166 persistently gave positive Wassermann reactions also. Seventy had received either insufficient or irregular treatment, 58 because of untoward reactions to treatment. One hundred patients were treated with bismuth. Negative serum reactions resulted in only two. Thirty were treated with an arsenical preparation, with no change in the serum reaction. Other groups were treated with metaphen, acetarsone, bismarsen, inhalation of ethyl iodide, and silver arsphenamine. It is emphasized that organic syphilitic involvement is in most instances the cause of persistently positive serum reactions and that such reactions usually mean uncured syphilis.

LANE, Boston.

INTERSTITIAL KERATITIS IN LATE CONGENITAL SYPHILIS. HARRY M. ROBINSON, South. M. J. **25**:956 (Sept.) 1932.

Interstitial keratitis is equally frequent in white and in colored people with late congenital syphilis.

A study of 144 patients with interstitial keratitis indicated that the diagnosis is often not made until irremediable corneal scarring has occurred. This may be due to failure to appreciate the importance of congenital syphilis in the etiology of this condition, to unfamiliarity with the common stigmas of late congenital syphilis or to failure to employ the Wassermann test of the blood as a routine diagnostic measure.

Adequate modern antisyphilitic treatment shortens the course of the acute inflammatory processes in interstitial keratitis, materially lessens residual corneal scarring, improves the ultimate visual acuity and lessens the incidence of relapse.

In interstitial keratitis which is originally unilateral, recurrence in the uninvolved eye may be prevented by adequate treatment in a high proportion of cases.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

DIAGNOSIS OF SYPHILIS BY MEANS OF A DESICCATED AND DEFIBRINATED DROP OF BLOOD. ALEJANDRO CHEDIAK, Arch. de med. inf. **1**:3 (Feb.) 1932.

The author has used this method in 254 cases. In these cases 49 positive reactions were obtained by a Wassermann test, 58 by a Kahn test, and 48 with the drop method. This method, therefore, closely approximates the results obtained by the other more elaborate tests. The blood is drawn from the lobe of the ear or from the toe. A drop is placed on a slide and defibrinated with a pinpoint. The remainder of the method is a process of complement and flocculation. The advantages are that it dispenses with venipuncture, which is difficult in infants and in fat persons, and that in urgent cases, such as those in which a transfusion is to be given, it gives an idea of the serologic state of the donor.

SANFORD, Chicago. [AM. J. DIS. CHILD.]

ERYTHEMA MULTIFORME: ARTHRITIS; BILATERAL ORCHITIS; ENDOCARDITIS; RÔLE OF ENTEROCOCCUS. J. HALLÉ, GIRARD and ODINET, Bull. Soc. de pédiat. de Paris **30**:413 (June 21) 1932.

A boy 12 years old, was admitted to the hospital with erythema multiforme, multiple arthritis and bilateral orchitis. On aspiration of the left knee, fluid was obtained from which enterococci were cultured. Aortic endocarditis developed. Two cultures of the blood were negative. The infection of the joints, testicles and heart was probably due to the same organism. The child showed no marked symptoms, but the lesions did not subside. His parents were instructed to keep him at rest in bed, and he was to be observed further.

BENJAMIN, Montreal, Canada. [AM. J. DIS. CHILD.]

TREATMENT OF SEVERE TYPES OF CONGENITAL SYPHILIS WITH BISMUTH. E. LESNE and LINOSSIER-ARDOIN, Nourrisson **20**:261 (Sept.) 1932.

In addition to extensive lesions of the skin and mucous membranes, these cases present marked involvement of the viscera, particularly the liver. Experience has taught that too vigorous early treatment with the arsphenamines is sometimes attended with disastrous results. To avoid this, the authors used fat-soluble salts of bismuth with gratifying results. The preparation employed was the camphocarbonate of bismuth, containing 0.01 Gm. of metallic bismuth per cubic centimeter. The average weekly dose was 0.5 cc. (0.005 Gm. of bismuth) per kilogram of body weight. Clinical and serologic cures have been rapid.

MCCLELLAND, Cleveland. [AM. J. DIS. CHILD.]

CUTANEOUS LEISHMANIASIS: CLINICAL AND HISTOPATHOLOGIC CONSIDERATIONS. G. FALCHI, Gior. ital. di dermat. e sif. **73**:1485 (Oct.) 1932.

The author presents a clinical and histopathologic report of four cases of oriental sore. The author believes that there is no essential difference between oriental sore and American leishmaniasis from the histologic, clinical and epidemiologic points of view, that these conditions should be grouped under the common heading of leishmaniasis and that the only distinction should be that usually made between different clinical forms of the same disease. As to the unity or plurality of Leishmania donovani and Leishmania tropica, there is not enough evidence on either side to solve this question satisfactorily.

THE GERSON-HERRMANNSDORFER AND SAUERBRUCH ACHLORINATED DIET IN TUBERCULOSIS: INFLUENCE OF SODIUM CHLORIDE ON EXPERIMENTAL TUBERCULOSIS OF THE RABBIT. G. BERTACCINI, Gior. ital. di dermat. e sif. **73**:1753 (Dec.) 1932.

The diet without sodium chloride recommended by Gerson, Herrmannsdorfer and Sauerbruch gives excellent results in many cases of tuberculosis. The author has endeavored to demonstrate the influence of sodium chloride on experimental tuberculosis in rabbits. One group of animals inoculated with bovine and human strains of the tubercle bacillus was placed on a salt-free diet and another group was given sodium chloride intravenously and by mouth. All the animals showed evidence of tuberculosis at autopsy, and no difference in the evolution of the process could be demonstrated in the two groups.

The author concludes that the experimental administration of sodium chloride to rabbits does not cause a diminution of the defensive powers against tuberculosis.

LUPUS ERYTHEMATOSUS TUMIDUS AND ERYTHEMA INDURATUM (BAZIN). M. COMEL, Gior. ital. di dermat. e sif. **73**:1812 (Dec.) 1932.

Comel reports a case of lupus erythematosus tumidus of the face and associated erythema induratum of the extremities in a woman in good general

health but in whom glandular tuberculous foci were demonstrated. From his studies of the histologic picture and particularly of the allergic reactivity, he concludes that the lesions were allergic tuberculids. He calls this type of cutaneous reaction "allergic secondary tuberculous microbids."

PARDO-CASTELLO, Havana, Cuba.

RECKLINGHAUSEN'S DISEAES. PEDRO PIULACHS, Progresos de la clin. **40**:469 (Aug.) 1932.

A case of Recklinghausen's disease is reported. A man, aged 53, presented various-sized fibromas and café au lait spots scattered in a bizarre manner over the body.

There was paralysis of the left upper extremity, which could not be attributed to a birth injury. The thenar and hypothenar eminences and the interossei and some of the flexor muscles were atrophied, producing claw-hand. However, the oculopupillary syndrome of Claudio Bernard-Horner, which frequently accompanies inferior radicular paralysis, was not present.

The right elbow showed limitation of motion between 90 and 120 degrees. Movement from the natural position of 100 degrees was accompanied by pain, especially severe on maximum flexion and extension. Roentgen examination of the right elbow showed exostosis, especially in the radiocubital articulation and in the superior portion of the olecranon process. The patient was below the average in intelligence.

The article is illustrated with clinical and histologic photographs.

CIPOLLARO, New York.

ERYTHEMA NODOSUM AND THE TUBERCULIN REACTION. DENES VON MORITZ, Arch. f. Kinderh. **93**:286 (June 16) 1931.

In ten cases of erythema nodosum, about a week after the disappearance of fever and nodules 0.1 mg. of old tuberculin was injected intradermally. A strongly positive reaction resulted in all patients, and in four of them a recurrence of the erythematous nodules followed. Several other experiments are cited in support of the view that the lesions of erythema nodosum are due to a sensitivity to tuberculin.

PALMAR AND PLANTAR KERATOMA IN COMBINATION WITH OTHER DEGENERATIVE SIGNS. GERTRUDE PALM, Arch. f. Kinderh. **93**:307 (June 16) 1931.

An 8 year old boy came under medical observation because of extreme thickening and desquamation of the skin of the palms and soles. At the site of desquamating patches of thickened epidermis the underlying skin was red and covered with abundant sweat of foul odor. The same condition had been present in four generations of the boy's family. A high arched palate also occurred in all members of the family exhibiting the hyperkeratosis. The condition is considered to be definitely inherited through the germ plasm and not affected by sex. Treatment is symptomatic.

LEMASTER, Evanston, Ill. [AM. J. DIS. CHILD.]

URTICARIA CAUSED BY HEAT AND COLD. KLEIN, Dermat. Wchnschr. **95**:1741 (Dec. 3) 1932.

Two patients were observed in whom urticaria was caused by the application of cold water. The author concludes that urticaria is a vasoneurosis rather than an allergic condition because (1) passive transfer of the sensitiveness failed, (2) no eosinophilia or leukocytopenia occurred during an attack, and (3) the potassium-calcium quotient remained normal.

THE RESULTS OF THE TREATMENT OF PSORIASIS VULGARIS WITH PLANT POLLEN EXTRACTS. G. SCHERBER and A. LUTTENBERGER, Dermat. Wchnschr. **95**:1749 (Dec. 3) 1932.

The authors tested nineteen patients with psoriasis with sixteen different pollen extracts applied by scarification. Increasing doses of the extracts to which the patients were sensitive were given. Three of the patients were markedly improved. Five showed no change. In the remainder, some degree of benefit was observed.

ZOSTER GENERALISATUS WITH LYMPHATIC LEUKEMIA. K. HAACK, Dermat. Wchnschr. **95**:1819 (Dec. 17) 1932.

In a 67 year old woman who had had symptoms of lymphatic leukemia for a year typical herpes zoster of the fifth nerve developed. There was an associated generalized varicelliform eruption. Arsenic had not been given.

ECZEMA DUE TO COLORED CHALK. BERNHARD KWIET, Dermat. Wchnschr. **95**:1827 (Dec. 17) 1932.

The author traced a dermatitis of the face and ears to irritation by the dust of colored chalk.

LIGHT AND AUTOBLOOD THERAPY IN LATE SYPHILIS, WITH PARTICULAR REFERENCE TO TABES. E. RAJKA and E. RADNAI, Dermat. Wchnschr. **95**:1839 (Dec. 17) 1932.

The authors obtained considerable subjective benefit in tabes by the use of erythema doses of ultraviolet radiation, combined with autohemotherapy.

CONVALESCENT SERUM IN LYMPHOGRANULOMA INGUINALE. FRIEDRICH KALZ, Dermat. Wchnschr. **95**:1839 (Dec. 17) 1932.

Three patients with early lesions and one with well developed lymphogranuloma inguinale were markedly benefited by the injection of serum from a patient who had recovered from the disease. Other known forms of therapy, including vaccine, had been found of little or no value in altering the course of the disease.

THE ENERGY METABOLISM IN SKIN DISEASES. P. BERGGREEN, Dermat. Wchnschr. **95**:1857 (Dec. 29) 1932.

The basal metabolism was determined in 204 patients with various cutaneous eruptions. The average values were rather close to normal except that in women with psoriasis they were a little high and in those with erythrocyanosis they were low.

THE GRENZ RAY TREATMENT OF ULCUS CRURIS. ERICH STEINER, Dermat. Wchnschr. **95**:1859 (Dec. 29) 1932.

The author reports that he obtained good results by treating a group of patients with varicose ulcers by means of grenz rays.

A CASE OF MELANOSARCOMA WITH MULTIPLE METASTASES INCLUDING INVOLVEMENT OF THE BUCCAL MUCOSA. J. E. VAN DER KAADEN, Dermat. Wchnschr. **96**:1 (Jan. 7) 1933.

The patient, a salesman 44 years of age, had a melanoma of the thigh. It was removed surgically twice, but recurred each time and gave rise to widespread metastases including a nodule under the tongue. At autopsy this nodule was proved microscopically to be melanoma. The author considers that the nevus cell is of mesenchymal origin and hence uses the term melanosarcoma. The treatment of choice for early melanoma is electrocoagulation extending well beyond the growth.

ATYPICAL GNAT BITE REACTIONS (CULICOSIS BULLOSA). H.-G. BODE, Dermat. Wchnschr. **96**:7 (Jan. 7) 1933.

Two sisters, 17 and 21 years of age, had bullous lesions on uncovered portions of the body, especially the legs. The bullae arose on a noninflammatory base, but a small erythematous halo developed later. The reaction apparently developed twenty-four hours after an insect bite, and bullae could be incited by the injection of an extract of Culex pipiens.

A CASE OF DERMATOMYOSITIS. ERNEST BENDER, Dermat. Wchnschr. **96**:13 (Jan. 7) 1933.

A 55 year old factory worker had had recurring attacks of arthritis for years. Infiltrated areas which varied from day to day developed in various muscles of the arms and legs. There was an associated polymorphous eruption, the lesions varying from those of erythema to pustular and hemorrhagic bullae. There was slight but persistent hyperpyrexia during the eight weeks' course of the disease. No eosinophilia or gastro-intestinal symptoms were noted. Marked leukopenia was present in the early stages of the disease.

TUBERCULOUS PRIMARY COMPLEX OF THE SKIN. RUDOLF BEZENCNY, Dermat. Wchnschr. **96**:58 (Jan. 14) 1933.

A 13 year old girl had a vesicular lesion on the cheek with associated enlargement of the local lymph nodes. The lesion on the cheek ulcerated and became indurated; clinically it suggested a chancre but dark-field examination showed no spirochetes. The blood count showed 4,200 white cells, of which 56 per cent were lymphocytes. The epicutaneous tuberculin test was strongly positive. There was no evidence of visceral tuberculosis. The ulcer was excised. Histologically it showed tuberculosis with many acid-fast bacilli. Three months after the excision typical lupus vulgaris developed in the scar. The case is considered an example of primary tuberculosis of the skin.

A SYPHILITIC CHANCRE OF THE EXTERNAL AUDITORY CANAL. KARL PREIS, Dermat. Wchnschr. **96**:67 (Jan. 14) 1933.

The author reports the case of a 34 year old soldier who had a primary syphilitic lesion in the external auditory canal. Spirochetes were demonstrated in the serum from the lesion.

CERTAIN OBSERVATIONS CONCERNING ECZEMA VACCINATUM (VACCINE GENERALISATA). G. STÜMPKE, Dermat. Ztschr. **65**:95 (Dec.) 1932.

The author reports four cases of children with eczema in whom vaccinia developed. None of them had been vaccinated, but they were infected by contact with other vaccinated children. In two of the cases the vaccinia appeared only on portions of the skin previously affected with eczema. In the other two the eruption also occurred on otherwise healthy skin. The recent literature is briefly reviewed.

DEVELOPMENT OF SARCOMA ON LUPUS VULGARIS. E. HESSE, Dermat. Ztschr. **65**:104 (Dec.) 1932.

Though the development of carcinoma on the basis of lupus vulgaris is relatively common, the development of sarcoma on this basis is extremely rare. The author reports the case of a 21 year old man with extensive lupus vulgaris of thirteen years' standing. He had received considerable roentgen therapy. In the area of lupus over the buttocks an ulcerative neoplasm developed which was shown microscopically to be a spindle cell sarcoma. Eighteen other cases from the literature are reviewed. In nine of these the patients had never had roentgen treatment.

MYOSITIS GUMMOSA OF THE STERNOCLEIDOMASTOID MUSCLE. GISELA SCHULTZE-WOLTERS, Dermat. Ztschr. **65**:124 (Dec.) 1932.

Syphilitic involvement of the muscles is unusual. It occurs in three forms: (1) diffuse myositis, (2) circumscribed gumma and (3) diffuse myositis with gumma. The first may occur in the early periods of the disease and usually affects the biceps or the gastrocnemius muscle. The second and third are usually seen in late syphilis and occur most often in the sternocleidomastoid muscle. Two patients, both women, were observed in whom gummatous myositis of the sternocleidomastoid had been treated surgically. In one the condition was made worse by the treatment. In both the process cleared under antisyphilitic treatment. The differential diagnosis of the condition is discussed.

EXPERIMENTAL INVESTIGATIONS OF LYMPHOGRANULOMA INGUINALE. FRANZ KOCH, Dermat. Ztschr. **65**:207 (Jan.) 1933.

As a result of his laboratory investigation, Koch shows that:

1. Guinea-pigs can be inoculated with lymphogranuloma inguinale, but the infection dies out shortly, owing to the natural resistance of this animal.

2. The mouse is readily infected, and the disease may exist for months though the animal remains apparently well. It causes a meningo-encephalitis and also involves the liver, spleen and lymph nodes, as can be shown by biophysical methods.

3. Monkeys are readily infected by intracerebral inoculation with the virus-containing material. Death occurs in a few weeks or months as a result of typical lymphogranuloma meningo-encephalitis.

4. By cerebral inoculation of a monkey with tissue from the lesions of a patient with estiomène (*Syphilôme anorectal*), meningo-encephalitis was caused. This further establishes the identity of esthiomène and lymphogranuloma inguinale.

THE LOCAL TREATMENT OF HYPERHIDROSIS WITH RESORCIN AND SALICYLIC ACID ESTER. ROLF FRIEDLÄNDER, Dermat. Ztschr. **65**:247 (Jan.) 1933.

A preparation consisting of one-third resorcinol and two-thirds salicylic acid ester has a keratolytic and tanning effect on the skin. The author advises applying it to hyperhidrotic areas once or twice a day for a few days. The treatment should be repeated in six or eight weeks. Of thirty patients treated, four were not benefited. The remainder had been relieved for from six to nine months.

INVOLVEMENT OF THE MUCOUS MEMBRANES IN DARIER'S DISEASE. A. SCHREINEMACHER, Dermat. Ztschr. **65**:311 (Feb.) 1933.

Two patients with typical Darier's disease were observed in whom lesions occurred on the gums. The lesions were slightly raised bluish-white spots. Biopsy of the lesions on the mucous membrane was performed in each instance. The histopathologic picture in both cases was similar to that of the eruption on the skin except that in one case the *corps ronds* were lacking. The author discusses the differential diagnosis.

THE PRECIPITATION REACTION IN THE SPINAL FLUID. R. FOERSTER, Dermat. Ztschr. **65**:326 (Feb.) 1933.

The citochol test of Sachs and Witebsky, as well as the Wassermann test, was made on 250 spinal fluids. There was complete agreement in 92 per cent of the cases. In 2 per cent the citochol reaction was more sensitive, and in 6 per cent the Wassermann was more sensitive.

THE DEMARCATION OF NEURODERMATITIS FROM CHRONIC ECZEMA ON THE GROUND OF CONSTITUTIONAL CONSIDERATIONS. ROBERT BRANDT, Dermat. Ztschr. **65**:330 (Feb.) 1933.

The author attempts to show that there are various constitutional differences between persons who have neurodermatitis and those who have chronic eczema. The work is based on the study of sixty-three cases of eczema and twenty-one of neurodermatitis.

TAUSSIG, San Francisco.

A NEW PROSTHESIS TO PREVENT LESIONS OF THE EYES BY ROENTGEN RAYS. E. WÖLFFLIN, Klin. Monatsbl. f. Augenh. **89**:214 (Aug.) 1932.

In his first publication (*Klin. Monatsbl. f. Augenh.* **82**:813, 1929) the author pointed out some disadvantages of his prosthesis against lesions caused by roentgen rays. These disadvantages have been overcome. The improved prosthesis consists of lead, 1.3 mm. thick, covered by galvanization with a very thin layer of cadmium, on which a cover of nickel is placed, also by galvanization. Secondary rays are almost entirely eliminated by this combination, which permits the use of the roentgen rays without resulting irritation of the interior or exterior surfaces of the lids. Rabbits' ears, exposed to very strong doses, showed no effect from secondary rays. The prosthesis, weighing only 10 Gm., is well tolerated by the patient's eyes for longer periods of time. It can be easily sterilized, does not break like the former prosthesis made of glass and may be perforated for local treatment of tumors of the iris.

STOLL, Cincinnati. [ARCH. OPHTH.]

THE ETIOLOGY OF ERYTHEMA NODOSUM. O. KREN, Wien. klin. Wchnschr. **44**:743 (June 5) 1931.

Erythema nodosum is not an infection *sui generis,* but a form of reaction to various acute and chronic infections, to bacterial and fungous invasions of the blood stream and even to chemical substances. The logical consequence of this is that in every case of erythema nodosum the cause of the symptoms should be ascertained in order to choose the correct therapy. The following causative factors are enumerated in the order of their importance: tuberculosis, syphilis, fungi, Trichophyton, lymphogranuloma inguinale and sepsis. The disease often follows angina, for such patients react promptly to vaccine obtained from angina smears, but not to preparations of salicylates or formaldehyde.

A NEW METHOD FOR EXTERMINATION OF HEAD LICE. L. V. WIKULLIL, Wien. klin. Wchnschr. **45**:175 (Feb. 5) 1932.

A new preparation named "Lausin" has been tried on three hundred pediculous children in convalescent homes with excellent results. It consists of 1 Gm. of yellow mercuric oxide in 100 Gm. of agar-agar. The mixture is shaken well before use and is left on for twenty-four hours. It is odorless, nonirritant and easy to apply.

DIETETIC TREATMENT OF CONSTITUTIONAL INFANTILE ECZEMA AND OF STROPHULUS. E. URBACH, Wien. klin. Wchnschr. **45**:496 (April 15) 1932.

The problem of infantile eczema is complicated and far from solution. Opinions of pediatricians in Germany and abroad as to the treatment are widely different and often contradictory. The author suggests that besides a local treatment, an etiologically based, dietetic therapy is highly important.

He divides infants into four groups, with regard to treatment: (*a*) In overfed infants the quantity of food is regulated in such a way that the weight increases slowly. This and the local treatment remove most of the eczema. (*b*) Atrophic or dystrophic children should be brought back to normal weight. (*c*) In the exudative type, the hydrolabile body consistency is brought back to normal by a salt-free and fat-free diet. An intracutaneous desensitization should be undertaken when the

cutaneous test shows an alimentary hypersensitivity. (*d*) Eutrophic children with eczematous conditions of the skin are treated by changing the intestinal flora, which causes changes in the excretion of acid.

Strophulus in infants and small children is almost always of a nutritive allergic nature. When the specific cause is discovered, the treatment by desensitization or a specific propeptone therapy should be instituted.

ABT, Chicago. [AM. J. DIS. CHILD.]

TRANSIENT CALCINOSIS UNIVERSALIS. H. JACOBOWITZ, Ztschr. f. Kinderh. **53:** 597 (Oct.) 1932.

The author describes a case of universal calcification of the soft tissues in a girl 4 years of age. The developmental history was entirely normal. She walked at 1¼ years. At 2 years she refused to walk and began to crawl. Two months before hospitalization, hard masses were felt in the soft tissues of the extremities, especially the knees. Roentgenograms showed that these masses contained calcium. Two months on a ketogenic diet and three weeks on sodium phosphate brought no relief; the masses became larger. After five months of hospitalization, fever developed and a rash appeared, which was thought to be erysipelas. After fourteen days the rash disappeared, but the areas over the calcic deposits became abscessed and excreted bits of calcium. The process continued for over three months, after which the abscesses healed and the calcic deposits disappeared.

SHELLING, Baltimore. [AM. J. DIS. CHILD.]

ZOSTERIFORM LICHEN PLANUS. S. P. ARCHANGELSKY, Sovet. vestnik venerol. i dermat., no. 7, p. 54, 1932.

The author reports the case of a 21 year old man who, for three weeks, had had a linear eruption 3 cm. wide on the flexor surface of the right upper extremity. It extended from the wrist to the acromion, where it split into two branches, one of which went along the first intercostal space to a point half an inch (1.2 cm.) to the left of the midline of the chest; the other branch extended along the upper edge of the right scapula and reached a point 1 inch (2.5 cm.) from the spinal column. The elementary lesion was made up of pale red or white papules, usually discrete but in some places grouped. Some of the lesions showed tiny vesicles. On the forearm, lateral to the linear eruption, there was a lesion the size of a half dollar consisting of hard papules of the acuminated type of lichen ruber. On both palms there were circumscribed sharply defined keratotic lesions which were scaly and fissured. Mild pruritus was the only subjective symptom.

The distribution corresponded to an area innervated by the fourth to seventh cervical nerves. Neurologic examination and general examination revealed nothing abnormal. Fungi were not found in the lesions.

After two weeks typical lesions of lichen planus appeared on the right forearm.

ERYSIPELAS AND PSEUDO-ERYSIPELAS IN PATIENTS WITH LEPROSY. G. P. MILASH, Sovet. vestnik venerol. i dermat., no. 8, p. 17, 1932.

The author describes four kinds of acute exacerbation in leprosy.

1. The appearance on the skin and mucous membranes of new lesions not associated with a constitutional disturbance.

2. Reddening and swelling of old lesions associated with moderate constitutional disturbance. This form occurs sometimes following treatment for leprosy and may be considered analogous to the Herxheimer reaction in syphilis. The first two forms may combine in the malignant type of leprosy which is produced by weakness of the immunobiologic properties of the organism.

3. Pseudo-erysipelas. The author has seen this condition in twenty-four cases. It starts with erythema and edema of diffuse lesions of leprosy, associated with

sudden rise in temperature, weakness, headache and insomnia. On the next day the lesions become more intensively red and swollen. Only the lesions on the face and on the extremities are affected, never those on the trunk or on hairy skin. The affected parts are not sharply defined; the erythema merges gradually into the normal color of the skin. In the affected parts bullae usually form which are filled with clear liquid containing lepra bacilli. The bullae break and leave extensive erosions. The prognosis in the majority of this group of patients is good. Often improvement takes place in the lesions of leprosy which have been affected with pseudo-erysipelas.

4. True erysipelas. In patients with leprosy true erysipelas seems to be rare. The author reports three cases. He differentiates this condition from pseudo-erysipelas by the sharp outline of the erythema, by the involvement of healthy skin (not only of lesions of leprosy), by the finding of streptococci in the bullae and by the contagiousness, which is seen by the appearance of the condition in several patients one after the other. In the three cases of erysipelas which the author has observed, one patient died of sepsis, and the two others were affected constitutionally more markedly than is usually seen in the patients with pseudo-erysipelas.

TREATMENT OF SOME DERMATOSES WITH DIATHERMY. S. M. KABATSHNIK and L. N. MASKILLEISON, Sovet. vestnik venerol. i dermat., 1932, no. 8, p. 21.

In the last three years the authors have used diathermy in the treatment of some dermatoses. The greatest number of patients treated by the indirect method (application of one electrode to the spine), with which the best therapeutic effects were obtained, had dyshidrosis and dyshidrotic eczema of the hands. Some of them had had the condition for four or five years. When the feet also were involved, the condition was considered as due to the epidermophyton, and such cases were excluded. The method consisted in applying a 6 by 8 cm. electrode to the region of the spine between the sixth cervical and second dorsal vertebrae and a 15 by 20 cm. electrode to the chest and using a current of from 0.4 to 1.2 amperes for from fifteen to thirty minutes. The treatment was given every second day for from ten to thirty treatments. Of twenty-two patients, fourteen were cured; in four the condition was considerably improved, and in four, moderately improved.

Local treatment with diathermy was used by the authors for the sclerodermalike infiltrations in acrodermatitis chronica atrophicans, in true scleroderma and in pernio. The small active electrode was applied to the affected part and the larger to the opposite side; a current of from 0.3 to 1.5 amperes was used for from fifteen to thirty minutes. From ten to thirty treatments were given, every day or every second day. In some cases another course of treatments was required after an interval of from one to two months. The improvement consisted in softening of the sclerodermatous or scleroderma-like infiltrations. In true scleroderma the thrapeutic effect was considerably less than in acrodermatitis chronica atrophicans. In all cases, however, arrest of the process was noticed. In pernio this treatment is recommended together with the usual therapy.

CHANGES IN THE REACTIVITY OF THE SKIN DEPENDENT ON THE MENSTRUAL CYCLE. A. A. KROITSHIK and A. I. LEBEDEFF, Sovet. vestnik venerol. i dermat., 1932, no. 8, p. 25.

The authors have made pharmacodynamic tests on 137 women by injecting intradermally 0.1 cc. of a 1 : 100,000,000 solution of epinephrine in physiologic solution of sodium chloride, and also a 1 : 10,000,000 solution of morphine in physiologic solution of sodium chloride. The tests were made seven days before menstruation, one to two days after the beginning of menstruation and seven days after menstruation had ceased. The investigations revealed that in the majority of women during menstruation the lymphagogue reaction (to morphine) is much more frequently present than the vasoconstricting reaction (to epinephrine). The former becomes

stronger as the menstrual period approaches, while the reaction to epinephrine weakens. The authors explain these facts by the hyperfunction of the ovaries during menstruation which is associated with hypervagotonia.

FACTS REVEALED BY FIGURES IN THE FIFTEENTH ANNIVERSARY OF THE GREAT OCTOBER. V. M. BRONNER, Sovet. vestnik venerol. i dermat., no. 9-10, p. 1, 1932.

The uninterrupted fight against venereal diseases during the last fifteen years has resulted in a distinct victory. In 1920, the first venereal dispensary was instituted, and in 1923 the first antivenereal expedition was sent out into the villages. In the last five years the number of venereal dispensaries and other antivenereal institutions increased from 55 to 200 per cent. A marked decrease in the registration of cases of syphilis was noted. At Moscow, for instance, the number of cases of all forms of syphilis registered for each 10,000 inhabitants, was 206 in 1913, and only 31.6 in 1931. The incidence of primary syphilis was 24.7 in 10,000 in 1913, and in 1931 it had decreased to 2.4. In 1917, one ambulatory dispensary registered 1,168 cases of primary syphilis; in 1931 all the venereal institutes in Moscow, which had a population twice as large, registered only 661 cases. The registrations in other cities showed similar figures.

In 1914, 56.9 per cent of the venereal patients were infected through prostitutes; in 1931, only 9.8 per cent. These figures indicate a marked diminution in the spread of disease through prostitutes.

INDIRECT ROENTGEN THERAPY IN CUTANEOUS DISEASES, PARTICULARLY IN LICHEN PLANUS. L. N. MASHKILEISON and L. A. FELDMAN, Sovet. vestnik venerol. i dermat., no. 9-10, p. 30, 1932.

The authors report their results in the treatment of lichen planus by the indirect method of Gouin. The method consists in irradiating the interscapular and lumbosacral regions with roentgen rays, using 140 kilovolts and 2 Holzknecht units filtered through 3 mm. of aluminum. One series consisted of three such treatments to each field at twenty day intervals. The interval between two series was not less than two months. The authors have treated nineteen patients with lichen planus in this way and consider the method one of the best.

In almost all cases pruritus disappeared after one or two irradiations. Although the localized forms of lichen planus responded to the treatment, the disseminated forms responded better and more quickly. In the majority of cases regression of the eruption was noted after one treatment. In some cases two irradiations of each spinal field were sufficient to make the eruption disappear. The hypertrophic and hyperkeratotic lesions on the legs also responded quickly. No relapse was noticed within six months after the treatment.

The mechanism probably consists in the effect of the rays on the sympathetic nervous system, which may influence one or several factors producing the dermatosis. No conclusion, however, can be drawn as to the exact etiology of the dermatosis.

BLOOM, New York.

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

R. L. GILMAN, M.D., *Secretary*

Friday, Dec. 2, 1932

F. D. WEIDMAN, M.D., *President*

DISSEMINATED TUBERCULOSIS OF THE SKIN. Presented by DR. D. M. SIDLICK.

A. S., a colored man, aged 28, a laborer, from Jefferson Hospital, presented an eruption on the face, neck, thighs, loins, buttocks, extremities, penis and scrotum, the lesions being of multiform character, consisting of macules, papules and papulosquamous and papulonecrotic lesions. Many were crusted, particularly those on the elbows and knees. The soles and palms were free from lesions. The size of the individual lesions varied from that of a pinhead to that of a small nodule. They were yellowish brown, and some appeared to be translucent.

The patient's physical examination showed nothing of interest. The Wassermann test of the blood was 4 plus. The condition had not improved under treatment with neoarsphenamine.

DISCUSSION

DR. C. S. WRIGHT: The condition looks the counterpart of that in a case which Dr. Klauder reported several years ago, a case of disseminated tuberculosis of the skin with papulosquamous lesions predominating. At first glance, of course, one might diagnose this condition as secondary syphilis, unless one is familiar with the type of case reported by Dr. Klauder. There is something about this type of case that is difficult to describe. We have seen two or three like it. I should make a diagnosis of tuberculosis of the skin, even without a report on the biopsy.

DR. HERMAN BEERMAN: About a year ago this man was admitted to the University Hospital. All the lesions were then the size of the small lesions on the neck. A biopsy from one of them showed typical tuberculous architecture, with many giant cells. Dr. Weidman thought the condition might be avian tuberculosis.

A CASE FOR DIAGNOSIS. Presented by DR. S. S. GREENBAUM.

M. S., an unemployed fire-tender, aged 33, presented an eruption of five years' duration on the scalp, chest, front and back, neck, arms and abdomen of numerous flat pink papules, crusted and scale-covered, especially those on the back. He had been well until five years previously, when an itching eruption had developed over the sternum, and gradually spread to the abdomen, back and head. Coincident with the spread of the lesions to the scalp, the patient's hair began to fall out. The condition had become steadily worse, with no remissions. Ten years previous to presentation he had contracted a primary lesion during army service and had received eighty-seven intravenous injections.

In addition to the areas mentioned, large, moist, confluent lesions appeared around the rectum, and the tongue showed several superficial lesions.

The patient did not perspire freely. His general health was good, except for constipation and frequent severe headaches. Physical examination showed poor dentition and a slow pulse. The blood pressure was 120 systolic and 86 diastolic. His mentality was poor. The reflexes were negative. He refused to have a Wassermann test made of the blood.

DISCUSSION

DR. W. O. ROOP: I suggest a diagnosis of seborrheic dermatitis, a very long, chronic case.

DR. D. M. SIDLICK: I am inclined to think that the condition is keratitis follicularis or Darier's disease. In many respects the appearance of the eruption corresponds to the description in a textbook. The disease has frequently been noted to appear on the face and head, and gradually to extend to and invade other parts of the body. At first the lesions resemble the color of the skin; later they assume the appearance of greasy-looking papules.

DR. J. M. SCHILDKRAUT: I think that the condition is Darier's disease.

SENEAR-USHER SYNDROME. Presented by DR. E. F. CORSON.

J. B., aged 42, single, from Jefferson Hospital, was, as an iron molder, exposed to intense heat and considerable dust. He was a confirmed drinker and smoker. An eruption suggestive of acne rosacea had been present on his face for a number of years, doubtless from the combination of habits mentioned. There had been a gradual change in the appearance of certain parts of the eruption in the last few months, though the patient was not sufficiently observant to note the beginning of the patchy, crusted, bat-wing outbreak on his cheeks and in front of and behind his ears. His lower lip was the seat of a fungating, crusted dermatitis such as is frequently noted with pemphigus. Its presence suggested the Senear-Usher syndrome. There was no eruption below the neck. There was no pulmonary disease or any other visceral disease, and the Wassermann reaction was negative. The teeth and mouth generally were much neglected as to hygiene.

DISCUSSION

DR. C. S. WRIGHT: Dr. Corson told me about how the man looked when he was first admitted, with heavily crusted lesions. At present, I should regard the condition as that of ordinary lupus erythematosus.

DR. E. F. CORSON: The lesions when first seen had crusted areas of rather significant shape, suggesting lupus erythematosus of both cheeks, with small areas in front of each ear. The patient gave a rather unsatisfactory history to the effect that he had had a rosacea-like condition on his face for seven or eight years, and that it gradually became transformed, giving the appearance seen at his admission. What suggested the Senear-Usher syndrome rather than lupus erythematosus alone was his lower lip, which had a fungating crust, with the crumbling appearance of healing pemphigus. While there were no distinct vesicles, the history suggested that there had been at one time. He has been in the hospital for six days, and the crusts have all come off in a fairly satisfactory fashion, but they left a deeper excavation than one would expect in lupus erythematosus.

DR. S. S. GREENBAUM: I shall subscribe to the diagnosis of lupus erythematosus for the eruption on the cheeks and behind the right ear, which has been present for years, but the patient gave me a history of another eruption suddenly developing on the lip, forehead and nose two or three weeks before this presentation. On examination I found that he had a fairly marked pityriasis capitis. I think that he has an acute infection on top of the lupus erythematosus, which is an infectious or toxic condition.

GRANULOMA ANNULARE. Presented by DR. ABRAM STRAUSS.

A colored man, aged 35, from Jefferson Hospital, presented a scalloped eruption at the nape of the neck. The Wassermann report was negative, but with antisyphilitic treatment the condition disappeared. A similar outbreak on the lips yielded only to roentgenotherapy.

DISCUSSION

DR. ABRAM STRAUSS: When this patient first presented himself, he had numerous annular lesions on the face and neck. A tentative diagnosis of secondary syphilis was made. Several of the lesions disappeared under antisyphilitic treatment, but those on the lips persisted, and from them the diagnosis of granuloma annulare was made. The lesions disappeared with roentgen therapy, but recurred in their present form. They were practically gone up to a month or two ago. The lip was most resistant to treatment.

DR. V. C. GARNER: Is the patient still receiving antisyphilitic treatment?

DR. ABRAM STRAUSS: No. This condition is of three or four years' duration.

LYMPHOGRANULOMATOSIS INGUINALIS. Presented by DR. FRANK CORMIA for DR. JOHN H. STOKES.

C. C., a young, white man, in good general health, presented a rather massive right inguinal adenopathy, which had eroded the overlying skin and formed a chronically discharging sinus. There were slight tenderness and slight involvement of the left inguinal glands. There were no other dermatologic lesions. The general physical examination gave negative results.

The Wassermann test of the blood was repeatedly negative. The patient was unmarried and admitted exposure previous to the appearance of the adenopathy. No lesions on the penis were noted at any time.

The patient received injections intradermally into the flexor surface of the forearm, of 0.1 cc. of known Frei antigen, obtained from Dr. DeWolf, of Cleveland, with 0.1 cc. of antigen prepared according to Frei's formula from pus obtained from the patient's suppurating glands and also with 0.1 cc. of similarly prepared antigen, obtained from the pus of another person with suspected but unproved lymphogranulomatosis inguinalis. A control injection of physiologic solution of sodium chloride with 0.025 per cent phenol was made. After forty-eight hours the results were read; the control test was negative. At the three other sites were raised, shotty papules, inflammatory and tender, with a white pustular top. These lesions had regressed somewhat, but were shown to illustrate a typical positive reaction to the Frei test.

The patient had received three intravenous injections of a solution of antimony and potassium tartrate, but there had been no clinical improvement at the time of presentation.

DISCUSSION

DR. S. S. GREENBAUM: I have seen five cases of lymphogranulomatosis inguinalis in the past two months, two of a very chronic type, of two or three years' duration, and three of acute or subacute type. In the chronic cases I could readily subscribe to the diagnosis of lymphogranuloma inguinale. In the subacute cases I was not so certain, because all three, though showing no history of a genital lesion, had the remains of a gonorrheal discharge. Gonorrheal bubo or staphylococcic bubo is not uncommon according to some urologists at the Philadelphia General Hospital, but to the general practitioner it seems very uncommon. In one of my cases cultures were negative, but smear examination showed a few cocci. When the lesions are open, it is difficult to verify the origin of positive cultures or smears. I think that it is difficult to differentiate subacute conditions, such as this patient has, from adenitis secondary to gonorrhea. That differential point is mentioned in only one of the papers that have recently appeared. For that reason only it is very difficult for me to subscribe to such a

diagnosis in this case. It may be that what we have been accepting as cases of adenitis secondary to gonorrhea are in reality cases of climatic buboes that we have heretofore not recognized.

DR. E. F. CORSON: I want to subscribe to what Dr. Greenbaum has just said. Although it does not appear in the history, the patient said that he had recently had gonorrhea, and that he still has a discharge.

I too, in my earlier days, worked in the urologic dispensaries, and I have seen conditions similar to this that were considered bilateral gonorrheal buboes. The bubo which is just beginning, that on the left, suggests bilateral gonorrheal bubo more strongly than the other, which has ruptured.

DR. D. M. SIDLICK: I have seen a fair number of complications as a result of gonorrhea in which the bubo showed signs of fluctuation and broke down more rapidly and extensively than in this case. I do not assume the attitude that I can tell the difference between the two lesions from the standpoint of this particular case, but this condition does not impress me as one of buboes which are the result of gonorrheal infection.

DR. S. S. GREENBAUM: In our second case pus was taken, and we made our own antigen of it. We tested three normal patients, none of whom reacted positively, but when we injected the antigen into a second and third patient with what we thought was lymphogranulomatosis inguinalis, a positive result occurred; one lesion was papular, and the other pustular.

DERMATITIS HERPETIFORMIS AND HERPES GESTATIONIS. Presented by DR. CHARLOTTE C. BACKUS, for DR. JOHN H. STOKES.

M. C., aged 35, a white American housewife, presented herself at the University Hospital on Nov. 28, 1932, with a pruritic, grouped, papular, urticarial and vesicular dermatosis, limited to the upper part of the back, the chest and the arms. On presentation, the urticarial element was much less pronounced, and there were signs of beginning pigmentation. The physical examination gave negative results.

The patient gave a history of having eight children living and well. One stillbirth occurred between the seventh and the eighth children. A second stillbirth occurred two weeks prior to the first visit to the clinic. Two days after the birth of the stillborn child, the dermatosis under discussion developed.

DISCUSSION

DR. R. L. GILMAN: I saw a case in Dr. Klauder's practice in which the dermatitis occurred about the sixth month of pregnancy. When previously pregnant, the patient had had a similar eruption, which disappeared. Both times she had a severe experience with early toxemia, and acting on a principle suggested by that fact, I treated her for three or four weeks with corpus luteum and noted a marked regression in the eruption. When the child was born, the eruption disappeared.

Except that these lesions show distinct grouping and pigmentation, I should hardly subscribe to the diagnosis given.

DR. A. STRAUSS: I should be more inclined to think that the condition was a toxic rash accompanying pregnancy, which we see every once in a while; the eruption lasts a few weeks or months, until the end of the term, at which time it disappears, and the patient never has a recurrence. Such certainly is not the case in true dermatitis herpetiformis. Of course, the location of the eruption favors a diagnosis of dermatitis herpetiformis.

DR. V. C. GARNER: When we saw this patient a week ago, the eruption was full blown, and there were a large number of subcuticular vesicles in the patches, and in the right axilla were two distinct bullous lesions. It is rather interesting that while most of the cases of herpes gestationis occur during pregnancy, occasionally an eruption appears directly after delivery. In this case, the child

was stillborn, and the eruption appeared a day or two after delivery. This case was shown at Dr. Stokes' clinic, and he unequivocally agreed to the diagnosis. The condition is so involuted that it is seen at a disadvantage tonight.

TWO CASES OF PSEUDOPELADE. Presented by DR. E. F. CORSON.

C. W., a white boy, aged 13 years, from Jefferson Hospital, presented areas of loss of hair on the scalp of two months' duration. The physical examination gave essentially negative results, save for some scattered folliculitis, small pitted scars and patchy alopecia.

A. C., a white Italian woman, aged 43, presented areas of loss of hair on the scalp. The case was of three years' duration (no definite history of folliculitis), and showed numerous disseminated areas of atrophic scarring with scaling.

DISCUSSION

DR. S. S. GREENBAUM: I think that the condition in the first case is too rapid a depilation for pseudopelade, and that the boy's condition is rather that of alopecia areata, since all the depilation occurred within two or three months.

DR. V. C. GARNER: I believe that the lesions presented by the woman are quite typical of the pseudopelade of Brocq. I was struck by the perifollicular redness which was particularly stressed in a recent monograph on the subject by Photinos. The morphology of the lesions, with the jutting out processes, is characteristic and quite different from that of the circular and ovoid patches of alopecia areata. Furthermore, if one is to consider this alopecia areata, how can one account for the atrophy?

DR. R. FRIEDMAN: I extracted a few hairs from around the border in the boy, and they were surrounded at the roots by a gelatinous substance that is characteristic of pseudopelade and that one does not find in alopecia areata.

DR. W. O. ROOP: It is possible that there may be two conditions present in this boy's infection. The lesions on the top of the head, to my notion, resemble more nearly pseudopelade, and the lesions on the side of the head resemble more closely alopecia areata. While we are, of course, more apt to think that one diagnosis will cover the entire case, it is quite possible that two conditions are present.

FOLLICULITIS ULERYTHEMATOSA RETICULATA OR CONGENITAL MILIA? Presented by DR. D. M. PILLSBURY.

A. F., a school girl of Italian parentage, aged 10 years, presented areas of atrophy scatteringly distributed over both malar prominences. The atrophic lesions varied in size from that of a pinpoint to 3 mm., and were separated by ridges of normal skin, which gave a somewhat reticulated appearance to the process, especially when viewed in cross-light. Near the borders of the involved regions were numerous milia and comedones, noted particularly in the temporal region and at the inner canthus of both eyes. There was a partial alopecia of the outer third of both eyebrows. The hair was somewhat dry and wiry, and there was a moderate partial alopecia in the frontal region and over the crown. In addition, there were generalized, widely scattered milia over the arms, trunk and legs, particularly over the back and thighs. The girl was rather poorly developed. The mother stated that the eruption had been present since birth, but she did not know whether the atrophic patches on the face were preceded by milia or comedones. There were no subjective symptoms.

The Wassermann test of the blood was negative; the basal metabolic rate, plus 7. No treatment had been given.

DISCUSSION

DR. V. C. GARNER: I am interested in asking Dr. Corson, who has published material on folliculitis ulerythematosa reticulata, whether he considers this a bonafide case. We were struck by the absence of the "reticulata" part of it.

DR. E. F. CORSON: It looks as though the same cutaneous structures are at fault in this instance as in the cases of naevus comedonicus, but, just as Dr. Garner says, here the pathologic condition is disseminated or scattered, instead of being grouped in a few patches. It is customary to consider the reticulated patches of folliculitis ulerythematosa reticulata as having a rather sharp margin, with sunken ridges running through them, greater depression to the patches and comedones and milium-like bodies embedded here and there in the patch. I cannot say that I can accurately catalog these lesions as that condition. The axillary appearance is worthy of note, approaching as it almost does an acanthosis nigricans by the pigmented appearance in that region and in the groin, possibly a juvenile type of that condition. Also the scalp should be noted. On account of the thinning of the hair and the possibly broken-off hair (there was a stubbly feel to certain parts) one might think of monilethrix, but the hairs had been examined, and that condition was not found.

ERYTHEMA INDURATUM, GRANULOMA ANNULARE OR PAPULONECROTIC TUBERCULIDS. Presented by DR. G. V. KULCHAR, for DR. JOHN H. STOKES.

M. D., a white American housewife, aged 34, presented when first seen in the dispensary of the University Hospital, on Oct. 24, 1932, dusky, red, indurated plaques of sizes varying from 1.5 to 3 cc. over the posterior surface of both legs. Some of the lesions were ulcerated, discharging purulent material. Physical examination gave otherwise negative results, except for surgical scars over the region of the anterior cervical glands on the right side. One month later a faintly erythematous annular plaque with raised and nodular borders appeared on the dorsum of the left hand. In the center of the lesion there was slight atrophy. Since observation there had been no change in the appearance of the lesion. Over the extensor surface of both arms and the dorsum of both hands were numerous scattered, pale, atrophic scars.

The Wassermann test of the blood was negative. Roentgenograms of the chest gave negative results. A biopsy was not performed.

In 1925, bilateral cervical adenitis had developed, which was diagnosed as tuberculous, and surgical drainage was done. Soon after this, numerous dusky red, large papules were excavated, and necrotic centers appeared over extensive surfaces of both arms and the dorsum of both hands. These lesions disappeared after four months and did not appear again until 1930, at which time they were diagnosed papulonecrotic tuberculids. At that time lesions developed over the dorsum of both legs similar to those visible at the time of presentation. They cleared up in three months, and there had been no recurrence until three months previous to presentation.

The patient had received six injections of gold sodium thiosulphate, followed by about 30 per cent involution in the lesions over the dorsum of the legs, though during this time the granuloma appeared on the dorsum of the hand.

DISCUSSION

DR. V. C. GARNER: I think we all recall at the Atlantic Conference the child with lupus erythematosus of the face, who at the same time had granuloma annulare of the fingers. The recurrent frequency of this association stresses the point, to my mind, that there must be some tuberculous relation in granuloma annulare, although it is one of the moot points in dermatology.

DR. R. L. GILMAN: I understand this patient came from the tropics, and that that was the source of her infection.

TUBERCLE OF CARABELLI IN A MOTHER AND THREE CHILDREN. Presented by DR. C. S. WRIGHT and DR. R. FRIEDMAN.

The mother, aged 31, married at 15. The father, aged 35, married at 19. They had eight children, all females; three were dead, and five were living. The first child, born prematurely at 7 months, died at birth; the second, born prematurely, at 6 months, was stillborn; the third, born prematurely, at 8 months, lived but one month. The other five children are living and, according to the parents, "have never been sick, except for measles, chickenpox and scarlet fever."

Marion, aged 7 years, sustained a fracture of the right radius on Sept. 1, 1932. While at Temple University Hospital she was found to have a 4 plus reaction to the Wassermann test. Wassermann tests were subsequently taken of her four sisters, father and mother. All were positive.

Carabelli tubercles were found on all five children, whose ages are 12, 10, 8, 7 and 4, and also on the mother. The right, upper first molar on the father was missing; no tubercle was present on his left upper first molar.

These patients were presented because of the occurrence of Carabelli tubercle in each of five congenitally syphilitic sisters and in their mother, who probably acquired her syphilitic infection from her husband.

DISCUSSION

DR. C. S. WRIGHT: Dr. Friedman and I thought it was unusual for an entire family to show this Carabelli tubercle. It is particularly of interest in view of the fact that the children have congenital syphilis, and the mother, acquired syphilis. It is generally agreed today that the tubercle of Carabelli is not in any way a suggestive sign of congenital syphilis, and we brought the patients here just to show that the tubercle is a hereditary characteristic not necessarily associated with syphilis.

DR. R. L. GILMAN: The tubercle in the left upper molar in the mother was of an abortive type, and this was true of each of the three children.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

H. J. PARKHURST, M.D., *Reporter*

Dec. 3, 1932

EMMETT C. TROXELL, M.D., *Presiding*

A CASE FOR DIAGNOSIS (MULTIPLE FIBROMAS? OSSEOUS CYSTS? ADENOMA SEBACEUM?). Presented by DR. CYRIL K. VALADE, Detroit.

Mrs. P. C., aged 25, has three children, the oldest of whom, aged 9 years, is just beginning to talk. She has two sisters, one of whom has a condition of the face and toes similar to that which she herself presents, while the other has involvement of the toes only.

At the age of 12 the patient noticed growths about the toe-nails, and later other manifestations appeared on the face and elsewhere. The evolution of the condition has been slow, with no subjective symptoms, excepting pain in the right great toe on pressure.

On examination, grouped about the nose and on the forehead, cheeks and chin, there was a moderate number of firm, pale, pinkish elevations which varied in size from that of a pinhead to that of a small pea. There were also three lesions on the eyelids and several on the left ear. Around and under the nails of all but three toes there were papillomatous growths of cartilaginous hardness, and

the nails of the first and second toes of the right foot were dystrophic. There was a small lesion on the right ring finger. Numerous small, elevated, pale, brownish lesions were scattered over the trunk. Several lesions the size of a split pea, with wrinkled surfaces, were grouped over the right posterosuperior spine of the ilium.

Roentgen examination revealed slight cystic changes in the bones involving the heads of the distal phalanges of the fourth and fifth fingers of the right hand with erosion of the distal phalanges of the great toes, especially the right one. The changes are considered to be entirely due to pressure by the papillomatous growths.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: A similar case was presented at the clinical meeting of the American Dermatological Association in Toronto in 1931; the diagnosis made by Dr. Wise was morbus Pringle, a name suggested by Urbach, of Vienna, for conditions presenting adenoma sebaceum and subungual fibromas.

DR. J. E. FISHER, Cleveland: The condition on the face is adenoma sebaceum, but the lesions on the trunk, together with the discolored areas, resemble those of Recklinghausen's disease. I suggest that this diagnosis be considered in addition to that of morbus Pringle.

DR. UDO J. WILE, Ann Arbor, Mich: Clinically the lesions on the face look much like those of adenoma sebaceum, but I was informed that biopsy did not confirm that diagnosis.

DR. H. L. KEIM, Detroit: Some of the sections show sebaceous hypertrophy.

ALOPECIA TOTALIS TREATED WITH AN ANTERIOR LOBE PITUITARY PREPARATION. Presented by DR. LOREN W. SHAFFER, Detroit.

H. T. P., a white man, aged 34, had alopecia areata in 1920. The process extended until in 1922 loss of hair was complete. During May and June, 1926, ultraviolet irradiation from the mercury vapor arc in quartz was used locally, and pilocarpine was injected into the scalp. Complete regrowth of hair followed. However, when treatment was discontinued alopecia recurred, and involvement was complete by March, 1927. During that year ultraviolet radiation, thyroid and arsenic were employed, without response. In November, 1931, treatment with an anterior lobe pituitary preparation was begun; 2 cc. was injected subcutaneously three times a week, and 5 grains (0.3 Gm.) was administered by mouth three times daily. This treatment has been continued constantly until the present time. In March, 1932, a growth of downy hair was noticed on the scalp. In August the growth was heavier and eyelashes had begun to appear. Since that time there has been little change.

DISCUSSION

DR. R. C. JAMIESON, Detroit: After seeing this patient I am reminded of one who came to me with mild premature alopecia, some time after the publication of the report on the treatment of baldness with pituitary. He followed the treatment closely and received injections two or three times a week. After six months the growth of hair was unaffected.

DR. F. M. JACOB, Pittsburgh: I have had the opportunity of studying thoroughly a case which occurred in an otherwise healthy girl employed as an assistant in chemical research. She had tried various remedies, without improvement. At my suggestion she tried glandular therapy, and she has received a large amount of this treatment, with no result.

DR. J. E. FISHER, Cleveland: Since reading Dr. Bengston's report I have had the opportunity of studying two cases, in which I have used about 200 ampules of an anterior lobe pituitary preparation, three injections a week being given, together with oral treatment. There has been no appreciable increase in the growth of hair, although one patient felt that his general condition had improved.

DR. O. M. GRUHZIT, Detroit: The amount that is generally used is very small. Possibly a larger dose might be more valuable. The ampules usually employed contain about 50 rat units, while in my experimental work in the laboratory of Parke, Davis & Co. I used much larger amounts. Perhaps 500 rat units would show a different result.

DR. E. W. NETHERTON, Cleveland: My associates and I had a patient who presented almost complete alopecia. Large doses of an anterior lobe pituitary preparation were used. There were terrific reactions, with nausea, vomiting and diarrhea. The treatment was continued for a long time with no benefit.

DR. J. E. RAUSCHKOLB, Cleveland: I raise the question of the hazards which might arise from the promiscuous use of large doses, such as the development of acromegaly.

DR. L. W. SHAFFER, Detroit: I am afraid that this treatment will go the way all cures for baldness have gone. I feel that there was some benefit in the case presented. A chemist informed me that the reactions are due to histamine, and it is practically impossible to make a solution of anterior lobe pituitary that is free from histamine. Some batches contain more than others. It is possible that, with increasing knowledge of sex hormones, larger doses can be given without danger and the reactions can be better controlled.

ALLERGIC ECZEMA. Presented by DR. ROBERT C. JAMIESON, Detroit.

O. W., a man, aged 58, a wood worker on automobile bodies, has handled wood as a cabinet maker for forty years. For twenty-five years he has had hay fever every summer; the condition was probably caused by sensitization to ragweed, but attacks have been precipitated by his working in contact with wood dust in a room without a ventilator. One brother has eczema, caused by sensitization to oatmeal.

In 1929 a maculopapular eruption of indefinite type appeared on the hips and buttocks; there was moderate pruritus. The same type of lesion appeared later on the arms and on the flexures of the forearms, producing an eczematous dermatitis. When he first came under my observation, in 1930, the arms, shoulders, thighs and waist were involved, with no definitely characteristic lesions. Acute outbreaks have occurred at irregular intervals; improvement has usually been noted when he was not working, but several recurrences took place when he was not at work. In 1930, he was presented at a meeting in Ann Arbor, where a tentative diagnosis of leukemia was made. His condition has improved greatly since that time.

On examination there were erythematous infiltrations around the nose, mouth and chin and excoriated chronic eczematoid areas around the thighs and buttocks. Neither the usual laboratory examinations nor biopsy revealed any abnormality. Sensitization tests with sawdust of various woods elicited positive reactions to ash and pine.

DISCUSSION

DR. G. H. BELOTE, Ann Arbor, Mich.: I believe that this patient was presented about two years ago, at one of the meetings of the Chicago Dermatological Society in Ann Arbor, as possibly showing pityriasis rubra pilaris. At that time the dermatitis was much more extensive. During the discussion, as I recall, lymphoblastoma was suggested. At present the condition seems to be simply chronic dermatitis.

DR. E. D. OSBORNE, Buffalo: I feel that this is a fairly characteristic case of dermatitis venenata, probably occupational. The condition shows the distribution typical of that eruption, and it cleared up when the patient was away from work for a time. He may have come in contact with stains, varnishes, turpentine and paints, which are common causes of dermatitis, and I wonder whether patch tests have been made with these substances. He may also have handled the crude oil which is used in polishing fine wood.

DR. H. J. PARKHURST, Toledo, Ohio: The patient states that he has done cabinet work only, and has not been exposed to oils, varnishes or other finishing materials. He has not worked for the past six months, and since the rash persists to some extent it seems possible that he may be sensitized to substances with which he comes in contact at home.

DR. R. C. JAMIESON, Detroit: He has never worked with oil. The fact that he has attacks at home leads me to feel that, in addition to the occupational factors, there may be some factor at home that precipitates the condition.

FOX-FORDYCE DISEASE. Presented by DR. ROBERT C. JAMIESON, Detroit.

M. K., a Jewish schoolboy, aged 15, states that ten months ago he noticed itching in the axillae and in the suprapubic area. This was soon followed by the appearance of a large number of minute, noninflammatory papules limited to these areas. In the suprapubic region, after repeated excoriation, the condition became eczematous. The papules are discrete, apparently all follicular, superficial and nonsuppurative, the eruption resembling a nutmeg grater. The patient is in excellent health, and no other person in the family is affected. Treatment has been entirely local and nonbeneficial.

FOX-FORDYCE DISEASE. Presented by DR. JOHN A. HOOKEY, Detroit, and DR. THOMAS H. MILLER, Detroit.

J. McW., a colored woman, aged 25, presents an intensely pruritic eruption of ten years' duration, affecting the axillae, breasts and pubic region. The itching is most severe when she becomes overheated. There is a discrete papular eruption, slightly darker than the surrounding skin. Laboratory tests gave negative results, and there was no evidence of tuberculosis. Sections showed a central area of hyperkeratosis, plugging the opening of a sebaceous gland, which had become cystic. In the same area there was a sweat duct which showed no pathologic change. There was mild perivascular lymphocytic infiltration. Sections fixed in alcohol revealed a more marked edematous change in the upper layer of the cutis and the epidermis, and in the deep cutis there was a group of apocrine glands showing pathologic changes. In the connective tissue septums there was a rather sparse lymphocytic infiltrate. For the most part the epithelium of the glands was separated from the supporting tissue, and the cells lying free in the lumen were largely destroyed. The changes were apparently confined to the coiled portions of the glands.

DISCUSSION

DR. L. W. SHAFFER, Detroit: In the first case the lesions lack certain characteristics which I think should be present in Fox-Fordyce disease, and there is not much itching. The fact that the disease is uncommon in males makes this diagnosis unlikely, and that of lichen nitidus should be considered. I think that unquestionably the second case is one of Fox-Fordyce disease.

DR. J. R. DRIVER, Cleveland: I agree with the diagnosis of Fox-Fordyce disease.

DR. E. W. NETHERTON, Cleveland: I subscribe to the diagnosis of Fox-Fordyce disease in both cases. I think that the lesions shown by the boy are characteristic, although, as Dr. Shaffer says, this condition is rare in the male. I had occasion to look up the literature on this disease, and found that a great preponderance of the cases reported occurred in females. The general feeling is that the condition is due to an endocrine disturbance.

DR. E. C. TROXELL, Detroit: I agree with Dr. Shaffer. In many cases this condition seems to have an endocrine basis.

DR. R. C. JAMIESON, Detroit: The fact that the onset occurred at puberty substantiates the endocrine theory. The boy, however, seems to show more signs of a possible endocrine change than the woman.

DR. T. H. MILLER, Detroit: When I first examined the boy it seemed to me that his bony structure and weight were somewhat feminine.

A Case for Diagnosis (Scleroderma with Cartilaginous Tumors?). Presented by Dr. Robert C. Jamieson, Detroit.

J. M., an Austrian, aged 52, employed in an automobile factory, was presented before the Detroit Dermatological Society twice in 1930 (Arch. Dermat. & Syph. **22**:751 [Oct.] 1930; **23**:200 [Jan.] 1931). The family history seems irrelevant. In 1900 an injury to his back produced a slight spinal deformity. Since that time he has had stomach trouble and some asthmatic attacks. His general health otherwise has been good.

In 1923 the dermal lesions appeared, first on the wrists and forearms, as groups of small, hard, white cartilaginous kernels. There were no subjective symptoms. The lesions later flattened and spread into areas which assumed a sclerodermatous appearance, with a tendency to the development of small patches of atrophy.

In 1929 similar lesions began to appear on the ears, the scalp, the mastoid areas, the nose and the forehead. They were small, white, waxy, semitranslucent nodules, very hard and showing no tendency to involution. The skin in general gave the impression of waxy infiltration.

On the elbows and knees the skin was extremely thick, hard and pachydermatous; when the extremities were extended the skin was thrown into deep, inelastic furrows. The same condition was present on the cheeks near the oral angles and over the nose between the eyes, producing permanent deep fissures and imparting a leonine expression to the upper part of the face. On the neck and shoulders there were masses of small, closely set, slightly reddened lichenoid papules. Above and below the knees there were large, well defined areas of pigmentation with some sclerodermatous changes. On the arms were a few areas which appeared to be softening and undergoing atrophy. The fingers were stiffened, the skin being waxy, sclerodermatous and atrophic. Epitrochlear and inguinal lymph nodes were palpable. The skin showed only the degree of anesthesia which might be expected to accompany these changes.

The blood pressure was 150 systolic and 80 diastolic. The blood sugar was 0.133 mg., the nonprotein nitrogen, 33 mg., and the cholesterol, 200 mg., per hundred cubic centimeters. The basal metabolic rate was —11. The dextrose tolerance was: fasting, 0.80; after forty-five minutes, 0.125, and after one and one-half hours, 0.111. The Wassermann reaction of the blood was negative. The erythrocytes numbered 3,820,000 and the leukocytes 8,800, with 77 per cent neutrophilic polymorphonuclears, 16 per cent large mononuclears, 5 per cent small mononuclears and 2 per cent eosinophils. The urine was normal. Roentgenograms of the skull showed a small-roofed sella turcica.

A small nodule removed from the ear was reported to be keratohyalin. In sections from the arm the pathologist found "an overgrowth of connection tissue and hyperkeratosis with keratotic whorls in the epidermis resembling deposits of calcium, but possibly consisting entirely of keratohyalin. The same deposits were found in the depths of the rete pegs."

The patient states that there has been an amelioration of the boardlike feeling of the skin during the past two years, and he can partially close his hands.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: I think that this case deserves extended discussion. It seems to furnish an excellent example of mimicry in dermatoses. At first glance, the nodular leonine appearance of the face suggested leprosy. But the feel of the skin is more like that in diffuse scleroderma, although I have never seen bony nodules in a frank case of scleroderma. I recall, however, that they have been described in the German literature. The possibility of leprosy can be excluded only by histologic examination. I should consider the condition scleroderma unless it is proved to be leprosy, which would not be surprising.

Dr. E. D. Osborne, Buffalo: Has a nodule been removed from the face?

Dr. R. C. Jamieson, Detroit: The only nodule removed was from the ear.

DR. E. I. STEINBERG, Erie, Pa.: It would be interesting to know whether this patient has received arsenic.

DR. R. C. JAMIESON, Detroit: He has not received arsenic, so far as I am aware; certainly not in the last two years.

DYSTROPHY OF THE FINGER-NAILS AND TOE-NAILS (SPOON NAILS). Presented by DR. WILLIAM G. WANDER, Detroit.

M. L. R., a girl, aged 9 years, the oldest of four children, weighed 4 pounds (1,814.37 Gm.) at birth. A younger brother is of mongoloid type, but the other children are normal. When she was about 2 weeks old her mother noted that her nails and hair were not growing properly. The past history is otherwise irrelevant.

I first saw the patient in 1930, at which time she had a congenital deformity of the finger-nails and toe-nails. The tips of the fingers and toes were keratotic and deeply fissured, bleeding readily. There was keratosis of the palms and soles, so painful as to interfere with walking. The nails were ⅛ inch (0.3 cm.) thick; they resembled pieces of coke or cinders, and the tips of the fingers and toes presented a charred appearance. The hair was brittle, dry and almost without pigment, and it had never attained a length that would permit curling. The teeth were poorly formed and widely spaced, and the gums, thick and spongy. The mentality was normal, and general physical development was good. The Wassermann reaction of the blood was negative. The basal metabolic rate was —47.

Tallow has been applied locally, and thyroid has been administered by mouth since 1930. Considerable improvement has ensued.

DISCUSSION

DR. J. R. DRIVER, Cleveland: This is another case of an endocrine disturbance concerning which little is known. Apparently the condition has improved under treatment with thyroid. Thorough investigation from that standpoint might throw light on the etiology.

A CASE FOR DIAGNOSIS (ACRODYNIA OR EPIDERMOLYSIS BULLOSA?). Presented by DR. ARTHUR E. SCHILLER, Detroit, and DR. WILLIAM G. SAUNDERS, Detroit.

M. D., a girl, aged 12, was presented, between 1926 and 1931, first before the Pittsburgh Dermatological Society and later before the Detroit society. Her mother is French, and her father, Italian. She is said to have been apparently normal at birth, and to have had rickets at the age of 11 months. At about that time there was an eruption, together with profuse sweating of the head, sore mouth and gums, abscessed teeth, diarrhea, pigmentation of the skin, anorexia, photophobia and head-burrowing. These symptoms persisted for several years, with improvement at times. There was complete alopecia at the age of 5 years and again at 10.

The hair is short, dry and sparse. The patient seems undernourished and presents a fairly generalized scaling and crusted dermatitis, the extremities, neck and inguinal regions being especially affected.

The erythrocyte count was 4,550,000, and the hemoglobin, 92 per cent. The leukocyte count was 6,800, 48 per cent of the cells being polymorphonuclear neutrophils, 1 per cent basophils, 49 per cent small mononuclears, and 2 per cent large mononuclears. The blood calcium measured 13 mg. per hundred cubic centimeters, and the blood sugar, 89 mg. The Wassermann reaction was negative. Roentgen examination revealed changes suggesting pulmonary tuberculosis. The histologic observations on biopsy sections were inconclusive.

EPIDERMOLYSIS BULLOSA. Presented by DR. JOHN A. HOOKEY, Detroit.

G. Z., a Jewish schoolgirl, aged 16, has had blisters, especially over bony prominences, since two days after birth. Lesions have appeared after trivial injuries,

and all of the nails are affected. Since 1930 there has been improvement. Areas of atrophy mark the sites of previous lesions. On the knuckles and dorsa of the hands there are several small papular lesions with white cystlike centers.

The basal metabolic rate was —22. Other routine laboratory tests gave negative results. Thyroid, calcium lactate and parathyroid have been administered, and there has been great improvement. Examination of histologic specimens has confirmed the diagnosis.

DISCUSSION

DR. H. T. PHILLIPS, Wheeling, W. Va.: The first patient was under my care from 1924 to 1927, and in 1927 I presented her before the Pittsburgh Dermatological Society. Diagnoses of pellagra, acrodynia and epidermolysis bullosa were suggested, the last mentioned being favored. There were lesions in the mouth and on the hands and feet. As she was underweight and undernourished, she was placed on forced feeding in the hospital, with temporary benefit. Improvement was also noted after the administration of thyroid.

DR. E. B. TAUBER, Cincinnati: In Cincinnati I have had under observation a Cuban family of five persons, all of whom have epidermolysis bullosa. One was highly susceptible to secondary infection, but under treatment with thyroid this tendency disappeared and the condition became ordinary epidermolysis bullosa.

DR. H. J. PARKHURST, Toledo, Ohio: I have seen the first patient before, and I feel that pellagra and acrodynia have been eliminated. The condition is probably atypical epidermolysis bullosa. I could find no small epidermal cysts, such as are present in the second case. The latter case is one of clearcut epidermolysis bullosa.

DR. J. A. HOOKEY, Detroit: I do not feel that the lesions in the first case are those of pellagra or of acrodynia, but the histologic picture seems to differ in the two cases.

DR. UDO J. WILE, Ann Arbor, Mich.: I consider the second case one of epidermolysis bullosa, but the first case does not seem to present that condition, at least in the form usually seen. It seems to me that the condition in this case belongs to the group of dystrophies known as congenital ectodermal defects, some of which are associated with definite glandular dyscrasia, such as has just been discussed.

DERMATITIS NODULARIS NECROTICA. Presented by DR. CHESTER A. DOTY, Detroit.

The case of R. S., a girl, aged 15, was reported in 1930 by Dr. Werner W. Duemling (Dermatitis Nodularis Necrotica, ARCH. DERMAT. & SYPH. **21**:229 [Feb.] 1930), who had observed the patient at Ann Arbor. In 1929, appendical pain was noticed, but operation was not performed. At that time "boils" appeared on the right buttock. They failed to heal, and others developed elsewhere. The original lesion healed about a year later. Some of the lesions ruptured spontaneously, exuding bloody serum. The condition, worse in winter, has persisted, gradually growing less extensive. Appendectomy was done in 1930, and two abscessed teeth were also removed. Other teeth were removed in 1932.

On examination, there were painless erythematous lesions, from ½ inch (1.27 cm.) to 2 inches (5.08 cm.) in diameter, on the extremities. Some were crusted, and some exuded a serous fluid. They were painless. The buttocks were also involved, and on the abdomen there were a number of superficial scars from the size of a small to that of a large coin. There was discrete cervical, inguinal, axillary and epitrochlear lymphadenitis.

The erythrocyte count was 3,800,000; the hemoglobin, 60 per cent, and the leukocyte count, 4,000. Cultures from the blood were negative, while those from pustules showed Streptococcus haemolyticus and Staphylococcus aureus. There was no evidence of tuberculosis. The Pirquet test and the Wassermann test were negative.

DISCUSSION

DR. J. E. RAUSCHKOLB, Cleveland: Possibly it would be well to rule out pulmonary infection with secondary involvement of the skin. Lowered resistance seems to play a part in this condition.

DR. H. F. DEWOLF, Cleveland: I was struck by the distribution of the lesions and the mental attitude of the patient, and I suspect that the condition is dermatitis factitia.

DR. W. R. JAFFREY, Hamilton, Ontario: I agree with Dr. DeWolf. Conjunctival and pharyngeal reflexes are absent.

DR. UDO J. WILE, Ann Arbor, Mich.: My associates and I observed the patient in the hospital in Ann Arbor for about a year, five years ago, and the results of our studies and tests were published. There was no suggestion of a factitious element, and we could not place the case in a definite category until we came across Werther's article, which appeared a few years ago in the German literature, describing an identical case as one of dermatitis nodularis necrotica. Since then we have had another case which I remember well in which for many years the condition was regarded as a destructive type of syphilis. I believe that this condition belongs in the same category as acne conglobata, which is not a distinct form of acne and affects areas where acne does not occur. This patient was thoroughly studied by Dr. Duemling, and the case was reported as one of dermatitis nodularis necrotica in 1929 at the meeting of the American Medical Association in Portland, Ore. This report was published in the ARCHIVES OF DERMATOLOGY in 1930 (**21**:229 [Feb.] 1930).

DR. H. T. PHILLIPS, Wheeling, W. Va.: I cannot agree with Dr. Wile, for I feel that the lesions are self-inflicted. The conjunctival and pharyngeal reflexes are absent, and the patient seems to enjoy occupying the center of the stage. At first she feels a small plug in the skin, and the lesions are apparently produced by her nails, which are unusually long. If the hands could be restrained so as to prevent scratching for two weeks, a diagnosis of dermatitis factitia could be definitely proved or disproved.

DR. F. M. JACOB, Pittsburgh: This condition differs in two respects from the usual form of dermatitis factitia: Apparently there has been definite improvement, and streptococci are present. I suggest a diagnosis of neurotic excoriation, for I believe that the lesions are accentuated by the patient's nervous nature and by picking.

DR. UDO J. WILE, Ann Arbor, Mich.: The patient was under observation in the hospital for a year, and during that time the nurses and staff should have discovered a factitial tendency. Her nails were kept reasonably short, and she was studied carefully. Therefore, I maintain that the lesions are not self-inflicted.

DR. E. W. NETHERTON, Cleveland: I do not regard the eruption as self-induced. The leukocyte count is low, and I wonder whether a tuberculous infection may be present.

DR. C. A. DOTY, Detroit: The patient has been under my observation since 1928, and during this period the condition has cleared up several times. My associates and I have been unable to find a diphtheroid organism, as was reported to have been done at Ann Arbor, although the staphylococcus and the streptococcus were found. I feel that diet and hospitalization are important.

LICHEN PLANUS SCLEROSUS ET ATROPHICUS. Presented by DR. ARTHUR E. SCHILLER, Detroit.

A. P., a Jewish housewife, aged 60, first noticed an eruption on the back, shoulders and clavicular areas about a year ago. The individual lesions are small, ivory-white papules with a glazed surface. There are tiny black plugs and areas of atrophy.

LICHEN PLANUS SCLEROSUS ET ATROPHICUS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

E. A., a woman, aged 24, first noticed small, whitish-purple, nonpruritic areas on her wrist about seven years ago. The eruption has spread gradually. Her mother has a similar eruption, and her father is alleged to have it also.

On examination the eruption was confined to the flexures of the wrists. It consisted of numerous atrophic, ivory-colored, flat-topped, polygonal papules from the size of a pinpoint to that of a glass pinhead, which had a violaceous sheen in tangential light. The lesions were umbilicated, but had no horny plugs. Some showed a fine white scale. No lesions of the mucous membranes were observed.

LICHEN PLANUS SCLEROSUS ET ATROPHICUS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

M. A., a married woman, aged 48, states that in September, 1931, she first noticed slightly pruritic whitish spots on both wrists. Lesions have developed on the neck within the past five months. She has had recurrent soreness of the mouth for years, which has not been treated. She has always been "nervous," and she was in an automobile accident two months before the onset of the eruption. Her daughter, who was just presented, has a similar eruption, and her husband is said to have the condition also, both cases antedating hers.

On examination, there were milky-blue and violaceous, radiating and glistening papules on the left border of the tongue, beneath the tongue and on the left buccal mucosa. On the nape and right side of the neck, the breasts, the flexor surfaces of the wrists and the inner surfaces of the thighs there were discrete and confluent, glistening white, umbilicated, flat-topped, polygonal atrophic papules from the size of a pinhead to that of a split pea, occasionally capped with a fine scale but with no horny plugs.

DISCUSSION

DR. F. M. JACOB, Pittsburgh: To see two cases of lichen planus in the same family, showing exactly similar scarring, is startling. The scarring of the lichen planus seems to be peculiar. In my own case of experimental lichen planus I found that the severity of the lesion did not seem to have any bearing on the scarring. Lesions on the back of my hand, which were negligible clinically, left a definite, though mild, atrophy, whereas other much more pronounced lesions healed without visible scarring.

DR. UDO J. WILE, Ann Arbor, Mich.: These cases are shown for two reasons: first, because it is unusual, at least in my experience, to find the condition in three members of the same family, and second, because there may be a question as to whether this eruption is true lichen planus sclerosus et atrophicus or lichen planus with atrophy. Because of the distinctly atrophic lesions on the nuchal region of the mother I doubt that these are cases of frank lichen planus.

DR. H. H. BAUCKUS, Buffalo: I have seen two cases of lichen planus occurring in members of one family.

DR. EMERSON GILLESPIE, Canton, Ohio: I have seen two definite cases of lichen planus in sisters.

BLASTOMYCOSIS. Presented by DR. UDO J. WILE, Ann Arbor, Mich.

A. T., a man, aged 49, injured his right ankle in January, 1932, while working on a farm. A painful nodule, which discharged pus, soon developed at the site of injury. To facilitate drainage and lessen the pain, the patient incised the lesion with a sterile pocket knife. About May, 1932, a granulomatous lesion appeared in the healing wound, which had not been treated.

On examination, there was a verrucous tumor, half the size of a palm, arising from the region of the right internal malleolus. It was raised a little less than 1 cm. and had a shelving, purplish-red border, which was rolled and studded with multiple, pinhead-sized, miliary, purulent abscesses, from which blastomycetes were easily and abundantly demonstrated.

Roentgenograms revealed an interesting condition in the chest. Biopsy specimens were examined.

Treatment has consisted of local roentgen irradiation and the administration of potassium iodide by mouth and of a solution (compound solution of iodine) intravenously, together with the usual local antiseptic measures.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: The case has no special interest from the standpoint of diagnosis, but is shown largely because a roentgenologic diagnosis of metastatic blastomycosis of the lungs has been made. My associates and I are unable to accept that diagnosis for the reason that the patient has been a coal miner. We feel that the lesions shown on the roentgen films do not justify a diagnosis of blastomycosis. The patient presents no general symptoms.

DR. C. K. HASLEY, Detroit: Roentgen examination showed extensive peribronchial involvement which, in all probability, was due to a widespread respiratory infection and was not associated with the cutaneous blastomycosis. When the lung is involved in blastomycosis the involvement spreads by way of the blood stream or the bronchi. The lesions usually seen are consolidated areas resembling patches of bronchopneumonia. The films submitted by Dr. Wile show more peribronchial infiltration, and since the condition involves both pulmonary fields rather than a particular area of one lung field, I feel that the findings in the chest are a coincidence. It is true that the infiltration of blastomycosis may be slight and fairly widespread, but in that case it usually simulates miliary tuberculosis. Also the fact that the condition in the chest remained stationary for several months seems to substantiate the opinion that the involvement is not due to blastomycosis, as one would expect a gradual extension. Furthermore, if blastomycosis were found both in the skin and in the lungs, one would expect to see much more evidence of metastatic involvement than this patient presents.

DR. R. A. C. WOLLENBERG, Detroit: Recently I had a patient with blastomycotic infection of the left cheek and the nose. He was in the hospital for over a year, under treatment with iodides and neoarsphenamine. The condition cleared up, but it recurred and responded readily to applications of carbon dioxide snow. The patient is now apparently cured.

MINNESOTA DERMATOLOGICAL SOCIETY

December 7, 1932

E. Z. SHAPIRO, M.D., *President, in the Chair*

ARSENIC-RESISTANT SYPHILIS. Presented by DR. C. D. FREEMAN, St. Paul.

H. S., a white man, aged 38, first saw the presenter in January, 1932, because of crusted lesions on the arms and thighs about 2 to 5 cm. in diameter. Following intravenous and intramuscular therapy, the lesions involuted, leaving pigmentation. About April 5, moist lesions began to develop, extending from the angle of the mouth. On admission of the patient to the University Hospital, in April, there were crusted lesions on the trunk and extremities. A course of malaria therapy was given. Tests of the spinal fluid gave negative results, but Wassermann tests of the blood have been persistently positive. The lesions involuted partially, and the patient continued therapy with mercury and silver arsphenamine. In August he was again referred to the University Hospital for a course of arsphenamine therapy. Seven injections were given, and also seven injections of neoarsphenamine. The crusted lesions have persisted, particularly on the extensor surfaces of the arms. There is still a moderate-sized lesion at the right angle of the mouth.

DISCUSSION

DR. JOHN BUTLER, Minneapolis: I think the lesions on the left arm are psoriasis, although the circinate lesions on the hand certainly suggest a serpiginous syphilid.

DR. H. G. IRVINE, Minneapolis: This man may not have chronic alcoholism, although he admitted drinking home brew daily. The only similar case I can recall, in which the lesions persisted, was one of alcoholism.

DR. S. E. SWEITZER, Minneapolis: I saw this patient at the time he was given malaria therapy, and I thought he had syphilis of a resistant type. I was of the opinion that he should have malaria or typhoid therapy and am surprised that the malaria treatment has benefited him so little. I believe he has only one disease, and I should be inclined to say that he has syphilis maligna.

DR. C. D. FREEMAN, St. Paul: This man was in the hospital for thirty days and did not have any liquor during that time.

DR. H. E. MICHELSON, Minneapolis: Cases of early syphilis that are resistant to arsphenamine, bismuth, mercury and malaria are rare. I saw a number of such cases exhibited before the Berlin Dermatological Society. Cases that are resistant to a combination of these types of therapy can be brought under control, I believe, by a carefully regulated dosage administered over a long period. What Dr. Irvine says about alcohol has some bearing on the case. I agree with Dr. Freeman that this is not the only factor. I believe that the condition will come under control, and I would not hesitate to continue the arsenic treatment over a long period.

NONPIGMENTED MELANOMA. Presented by DR. H. E. MICHELSON, Minneapolis.

The patient, a man aged 52, was treated with a cautery in September, 1932, for a keratosis on the left cheek. In October, 1932, while harvesting corn, he injured the area with a corn stalk, and it immediately became elevated. It presented a circumscribed lesion, deep red, soft and the size of a cherry. It bled easily. A tentative diagnosis of pyogenic granuloma was made, and the lesion was shaved off and cauterized at the base. The microscopic diagnosis, made by Dr. Bell from examination of the removed tissue, was nonpigmented, malignant melanoma.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I think that diagnosis is correct.

DR. H. E. MICHELSON: In every odd type of tumor of the skin, one should always consider sarcoma. There is no question that in this patient the history and the type of lesion pointed to pyogenic granuloma as the most probable diagnosis. Unfortunately, the microscopic picture is of a highly malignant, nonpigmented melanoma. Dr. Peyton is going to make a wide excision, not with the hope of cure, but because he thinks that primary union is the sensible procedure in this type of case, owing to its psychic effect.

EPITHELIOMA OF THE EYELID. Presented by DR. C. D. FREEMAN, St. Paul.

The patient, a man aged 50, has a lesion on the upper left eyelid. It is a small ulcer, half a centimeter in diameter, and has been present about six months. A biopsy has not been made. The case is presented for suggestions as to therapy.

DISCUSSION

DR. JOHN BUTLER, Minneapolis: I think a basal cell lesion near the inner canthus should be treated surgically. I would not use radium on it except as adjunct treatment. Where there is involvement of cartilaginous tissue, radium is not always effective.

DR. H. E. MICHELSON, Minneapolis: I recommend that a small piece of the involved tissue be taken for biopsy because the possibilities include not only the three ordinary types of epithelioma, but glandular carcinoma and melanoma. If the biopsy should show a highly malignant growth, it will be necessary to sacrifice the bulbus and do a widely destructive operation. In case the lesion is of low grade malignancy, treatment with irradiation will suffice.

DR. JOHN F. MADDEN, St. Paul: Six years ago I saw a patient who had an epithelioma in about the same location. This was treated by Dr. Irvine with radium. I saw the patient again last month, and the cosmetic and therapeutic results were excellent.

DR. H. G. IRVINE, Minneapolis: I remember the case Dr. Madden mentioned, but, as I recall it, the cartilage was not involved.

DR. C. D. FREEMAN: I think the way to treat this condition is with roentgen rays. I do not see how it is practical to treat it with radium. If operation is done, there will be danger of xerosis of the eyeball or eversion of the lid and ultimate loss of the eye. A conservative method will not make the ultimate prognosis worse, and operation can always be resorted to, if necessary.

DR. S. E. SWEITZER, Minneapolis: I think the lesion has not yet involved the cartilage, and that it could be treated successfully with roentgen rays.

A CASE FOR DIAGNOSIS. Presented by DR. H. G. IRVINE and DR. D. D. TURNACLIFF, Minneapolis.

J. G., a woman, aged 16, states that four years before presentation a wart was excised in the location of the present eruption. The physician who made the excision reported that the lesion removed was of the verruca vulgaris type, about the size of a pea, and that the surrounding skin at the time of operation was entirely normal. A slight scar is now evident on the back of the right ear. The patient does not know when the present eruption started. It is on the back of the right ear and extends to the mastoid area, occupying a surface about one quarter to three eighths of an inch wide and about an inch long. The eruption is composed of milia-like lesions, rather closely packed but remaining discrete. An unsuccessful effort to remove them as one would milia indicates that they are not encapsulated and cannot be pressed out; nothing but blood comes from the incision. There has been no extension or change during the six weeks that the patient has been under observation. A few lesions at one end of the area have been touched lightly with the cautery, and this appears to give a satisfactory result.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I am willing to make a diagnosis of sebaceous nevus of Jadassohn. This condition has been described often in the German literature, and recently in the ARCHIVES. The treatment is simple, consisting of excision or acucautery.

DR. JOHN BUTLER, Minneapolis: I should make a diagnosis of lymphangioma circumscriptum. The treatment that Dr. Irvine has instituted will clear it up successfully as a rule. Of course, there will be scarring.

DR. S. E. SWEITZER, Minneapolis: I think it is nevus sebaceus of Jadassohn, and the treatment I recommend is cautery.

CONGENITAL ECTODERMAL DEFECT, WITH MILIA. Presented by DR. S. E. SWEITZER, Minneapolis.

F. F., a girl aged 9, has never had any hair on her body, except an occasional hair on her scalp. At the age of 6 months, small lesions the size of pinheads appeared on the elbows and knees and gradually increased in number. They have

been present on the face since she was 1 year of age. The teeth have always been normal. There has been no serious illness. One brother had the same condition, though it was less severe. The mother and father are both living and well.

Examination showed the girl to be well nourished. There was no hair on the body, and the eyebrows, eyelashes and hair of the scalp were completely absent. The teeth and nails appeared normal. Over the face, scalp, neck and extremities (especially the knees and elbows) were hundreds of pink or white papules the size of a pinhead. There has been no response to any therapy. Biopsy showed milia.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I was under the impression that a patient with this condition does not perspire. This child was perspiring freely, especially in the axillae.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. S. E. SWEITZER, Minneapolis.

The patient, a well developed woman, aged 36, has had two pairs of twins and three other children, and has always been well. She stated that five years before presentation, previous to the delivery of twins, her legs became purplish red, and the doctors believed the condition was caused by varicose veins. During the past winter the condition became worse, and now involves and is limited to both legs below the knees. Examination showed the skin to be somewhat reddened and mottled and slightly thinner than normal. Small veins were visible beneath the epidermis. A biopsy section is shown.

DISCUSSION

DR. S. E. SWEITZER: I have had several cases of acrodermatitis chronica atrophicans in which venous injections have been made without previous diagnosis.

DR. H. E. MICHELSON, Minneapolis: It is surprising to note how many patients with acrodermatitis chronicus atrophicans are subjected to venous injections. Such cases are reported before societies all over the world.

KERATOSIS FOLLICULARIS. Presented by DR. H. E. MICHELSON, Minneapolis.

J. C., a white woman, aged 17, stated that at the age of 8 she had first noted an eruption on the palms and soles, which disappeared with local treatment. It recurred and gradually became worse, spreading to the face, neck and chest. The eruption consisted of brown, keratotic papules the size of pinheads. There were scaling, plaquelike lesions on the soles and palms. The patient also had an associated acne vulgaris, which responded well to the usual treatment. On the palate were noticed a group of small white-celled papules.

DISCUSSION

DR. L. H. WINER, Minneapolis: I was interested to see the condition clear up so successfully under roentgen treatment. Professor Kren presented a case before the Wiener Dermatologische Gesellschaft in the spring of 1930; the condition cleared up with the use of grenz rays.

FUNGUS INFECTION OF THE MOUTH AND SKIN. Presented by DR. H. E. MICHELSON, Minneapolis.

F. R., a white woman, aged 18, presents an eruption that began in the mouth about ten years before presentation and gradually spread, involving the fingers and, when seen four years ago, the face. The course has been variable. The lesions have never entirely disappeared. Cultures showed a growth of Oïdium.

Because of a depressed nasal septum and developmental anomalies of the teeth, repeated Wassermann tests of the blood were made, as well as one of the spinal fluid. All the results were negative. The results of tests made on the parents were also negative.

DISCUSSION

DR. A. F. HALL, JR., Fort Wayne, Ind. (by invitation): I understood one of the doctors to say that he had been through most of the pharmacopeia trying to find something with which to treat the condition. The society of Fort Wayne was addressed by a medical missionary from India, who stated that tincture of iodine was administered intravenously in some of the men mauled by Bengal tigers, and that later it began to be used for many other conditions, from fungus infection to syphilis. He reported good results in the tropical diseases. As I recall, the procedure is to start with 2 minims of iodine (0.12 Gm.), diluting it to 2 cc. I suppose this method has been reported. If everything else has been tried in this case, and if the proper technic for the treatment with tincture of iodine can be learned, it might be tried.

LICHEN PLANUS OF THE LIP. Presented by DR. H. G. IRVINE and DR. D. D. TURNACLIFF, Minneapolis.

A man, aged 26, presents a thin, irregularly outlined, grayish film on the lower lip, with one area, the size of a pea, slightly thickened and of a deeper color. This condition had existed on the lower lip during six months of observation before other evidences of lichen planus developed in the mouth, on the penis and on the leg below the knee. Previous to the development of the other lesions we were unable to make a diagnosis.

MULTIPLE GANGRENE OF THE SKIN FOLLOWING SCARLET FEVER. Presented by DR. S. E. SWEITZER, Minneapolis.

H. K., a well developed boy, aged 6, had two ulcers on the right cheek, one on the right side of the neck and one on the right side of the chest. All were about the size of a half-dollar and were gangrenous. The floors of the ulcers were composed of granulation tissue, the edges were deeply undermined, and there was continuous purulent drainage. A biopsy section was shown.

The patient had scarlet fever in May, 1932, complicated by tonsillitis, cervical adenitis and an abscess of one of the right molars. Sinuses developed on the right cheek and neck, which drained during the entire summer of 1932. A culture showed hemolytic streptococci. In July, 1932, a pustule developed on the anterior surface of the chest, which increased in malignancy and became gangrenous. At all points previously mentioned on the chest, neck and cheek, surrounding areas of gangrene the size of a half-dollar developed. There was no tendency to spontaneous healing. The patient has improved markedly under therapy with vaccine, ultraviolet rays, antiseptic wet packs and repeated grafting of skin.

DISCUSSION

DR. S. E. SWEITZER: This condition was described in the ARCHIVES recently under a wrong name — dermatitis gangraenosa infantum. We call the condition ecthyma gangraenosum. Multiple gangrene following scarlet fever is rare. The history shows a hemolytic streptococcus in the lesions. The condition is slow in responding to therapy.

DR. L. H. WINER, Minneapolis: As Dr. Sweizer says, the hemolytic streptococcus was considered to be the cause of these ulcers and was cultured from them, whereas in ecthyma gangraenosum, Bacillus pyocyaneus is usually found in both smears and cultures.

LOS ANGELES DERMATOLOGICAL SOCIETY

L. F. X. Wilhelm, M.D., *Secretary*

Regular Monthly Meeting, Dec. 13, 1932

Samuel Ayres, Jr., M.D., *in the Chair*

Abnormal Psoriasis. Presented by Dr. Irving R. Bancroft.

H., aged *32*, presents an eruption on the soles which has been present for several months. This eruption resembles mycotic dermatitis. The edges are red, sharply marginated and somewhat circinate. There has been practically no scaling. The finger-nails are definitely punctate. The patient had no other eruption until five weeks before presentation. While he was in bed with influenza, a diffuse, papular eruption suddenly developed, chiefly over the abdomen, legs and arms. At present these papules are less than 1 mm. in diameter, and some of them are covered with silvery scales. The condition has been diagnosed as psoriasis.

DISCUSSION

Dr. William Goeckerman: This is a rather striking case from a morphologic standpoint. I, too, would diagnose it as psoriasis. I think the plantar involvement is psoriatic. The configuration is somewhat bizarre, but not so much so but that it fits in with the diagnosis. It must be remembered that psoriasis is capable of producing unusual manifestations. I was interested in the febrile attack. Psoriasis often follows in the wake of a febrile attack such as that accompanying acute tonsillitis, tonsillar abscess and influenza and even that following the removal of teeth. While this does not necessarily establish an etiologic relationship, it may be that the febrile attack acts as a precipitating factor in a predisposed person.

Dr. Michael L. Ravitch: I think the eruption on the body is typically that of psoriasis; more noticeable are the psoriatic scales on the scalp.

Dr. Stanley O. Chambers: I am interested in the possible relation between the frank dermatomycosis between the toes and the development of the papular psoriasis. The clinical characteristics of psoriasis are mingled freely with those of the dermatomycosis.

Dr. Nelson P. Anderson: I believe this is a case of psoriasis. When I first saw it, I believed it to be lichen planus. The thimble-like stippling on the nails is evidence in favor of psoriasis. The fact that practically the entire nail is involved indicates that the patient had psoriasis for a long time before the eruption appeared on the skin. The nails are involved to the tip, and nails do not grow in five weeks. I would say that the febrile attack did not cause the psoriasis, but that it in some way aggravated the condition and produced the eruption on the skin.

A Case for Diagnosis. Presented by Dr. H. C. L. Lindsay.

S., aged 47, has had a purpuric rash on the lower extremities, hips and waist for several years. It is inflammatory to a mild degree and itches slightly. He has been treated with suprarenal extract in one of Lassar's paste, with surprisingly quick improvement. The lesions do not look like Schamberg's disease, and they are not nevoid. No biopsy has been made. The patient is in good health except for the condition of the skin. However, in the past he suffered from hypertension and toxic myocarditis. The Wassermann test of the blood gave negative results.

DISCUSSION

Dr. Samuel Ayres, Jr.: I saw on one leg what appeared to be an area of superficial atrophy. One could almost feel where the normal skin began and thinning took place. I thought at first that the disorder was due to a condition of stasis, but I believe a slight atrophy could be detected in one place.

Dr. Stanley O. Chambers: A diagnosis of stasis dermatitis seems unavoidable. No atrophy, vascular tufts, annular configuration or pigment characteristics of Majocchi's disease are evident.

Impetigo Herpetiformis. Presented by Dr. Samuel Ayres, Jr.

C., a Negro, aged 37, was shown before the dermatologic staff of the Los Angeles General Hospital two weeks ago. The eruption had been present about three weeks. The patient stated that shortly before the outbreak he had eaten a large quantity of chitterlings, a delicacy made of hog's intestines. The patient did not feel particularly ill. The eruption was strikingly symmetrical, involving especially the neck, the axillary regions anteriorly and posteriorly, the thighs, especially near the crotch, the bends of the elbows and scattered areas on the trunk. The lesions were grouped and consisted of extremely superficial, flaccid vesicles and blebs, varying in size from that of a pinhead to that of half a dime. These strongly resembled impetigo, yet the grouping and distribution were more typical of dermatitis herpetiformis. The eruption cleared up rapidly with wet boric acid dressings. Yesterday, however, the patient returned to the outpatient department with an exacerbation of the eruption. There were definite peripheral crusting and bleblike vesiculation, although the previously active areas were quiescent. Several discrete new blebs were present. Each of these was flaccid and superficial, and the lower two thirds of each lesion was occupied by gravity pus. Pemphigus should be considered. Although impetigo herpetiformis is rare in the male, it has been recorded, and the eruption in this case strongly suggests this diagnosis.

DISCUSSION

Dr. William Goeckerman: I have not had much experience with dermatoses in the colored race. Those who see a great deal of them practically admit they are almost as often wrong as right in their clinical impressions. I believe the eruption looks like pemphigus foliaceus.

Dr. Michael L. Ravitch: Was examination of the blood made? Is there any itching?

Dr. Samuel Ayres, Jr.: The Wassermann reaction was negative. There is little itching.

Dr. Kendall P. Frost: I should be inclined to sidestep so explicit a diagnosis as either pemphigus foliaceus or impetigo herpetiformis at present. I should call the condition a bullous toxic eruption and await developments before becoming more explicit in the matter of diagnosis.

Dr. William Goeckerman: The patient did not have the Nikolsky sign.

Dr. Samuel Ayres, Jr.: I do not believe that this is true dermatitis herpetiformis. The earliest and smallest lesions were pustular from the beginning, and lesions no bigger than a pinhead have creamy pus in them. That would also tend to exclude pemphigus. I do not believe it is impetigo. The eruption has the symmetry of dermatitis herpetiformis, but the lesions are like impetigo. All the vesicles in each lesion have superficial gravity pus filling the lower two thirds of each bleb. No biopsy has been made.

Dr. Stanley O. Chambers: One or two cases of keratosis blennorrhagica have been described which almost fit this picture. An investigation for possible gonorrheal foci would be interesting.

NEW ENGLAND DERMATOLOGICAL SOCIETY

WILLIAM P. BOARDMAN, M.D., *Secretary*

Regular Quarterly Meeting, Dec. 14, 1932

ARTHUR M. GREENWOOD, M.D., *Presiding*

TOXIC DERMATITIS. Presented by DR. BERNARD APPEL.

L. McL., a Canadian woman, aged 25, a stenographer, from the skin department of the Boston City Hospital, had had secondary syphilis six years previous to presentation. She received about thirty injections of arsphenamine and thirty of bismuth; after this treatment, tests of the blood and spinal fluid for syphilis were negative. She received the last treatment about two years ago. The patient is pregnant from seven and one-half to eight months. Four months ago an eruption developed which was generally distributed, fairly symmetrical and discrete, with slightly raised maculopapules from 5 to 15 mm. in diameter, brown pigmentation and occasional scaliness, which was not silvery. The new lesions are slightly pinker than the old ones. The old lesions are dryer but not scarred. An occasional excoriation is seen.

The Kahn test was negative twice; the Wassermann reaction and the Hinton reaction were negative. A blood count showed 3,260,000 red cells, 44 per cent hemoglobin and 5,200 white cells. A blood smear showed essentially secondary anemia. There was a slight trace of albumin in the urine.

The patient was treated with iron and ammonium citrate, and with the ointment used in the Danish treatment of scabies.

DISCUSSION

DR. W. P. BOARDMAN: It seemed to me that the lesions on the extensor surfaces are grouped and somewhat circular in arrangement, and I suggest a diagnosis of toxic erythema due to pregnancy; some of the lesions suggest erythema multiforme, but they are too persistent. In some cases the condition resembles dermatitis herpetiformis, but in others it is like erythema multiforme, but instead of lasting for a certain period, the lesions persist until the end of pregnancy and then clear up.

DR. C. GUY LANE: It seems to me that dermatitis herpetiformis should be considered, but as I examined the patient I wondered whether the condition should be classed with the group of cases of pityriasis lichenoides varioliformis acuta that Senear and Oliver have reported. I have seen one or two patients with this condition; the lesions are fairly widely distributed, usually papular and sometimes rather firm, and sometimes contain a large amount of pus and leave scars. Some of the lesions suggest pityriasis rosea during certain stages, and yet they are apparently deep enough to produce scars. I think that this group of conditions ought to be considered in this type of case.

DR. A. M. GREENWOOD: Dr. Lane and I saw such a case last year. This case fits in admirably with pityriasis lichenoides varioliformis acuta. I followed the patient with this condition for several weeks, and there were no generalized lesions. It was difficult at one time to distinguish the condition from syphilis. The patient was a man.

DR. B. APPEL: I think that vesicles should appear during the course of dermatitis herpetiformis.

KYRLE'S DISEASE (?). Presented by DR. JOHN G. DOWNING and FRANCIS P. MCCARTHY.

G. W., an American woman, aged 31, has had sores on the anterior surface of the lower part of the legs, which occasionally itch and occasionally heal and

leave scars, for the past three years. The patient shows two lesions on the lower part of the right leg and three lesions on the lower part of the left leg; the sites of previous lesions show smooth noncontractile scars. The lesions start with definite follicular plugs grouped together. The largest lesion is about 1 cm. square and has a verrucous appearance with a definitely infiltrated base.

The Wassermann reaction was negative. Biopsy showed large keratotic epidermal plugs, atrophy of the epidermis, disappearance of pegs and growth of young connective tissue in the derma, with increased vascularity and a pronounced infiltration of round cells. The Kahn test was negative.

DISCUSSION

DR. J. G. DOWNING: I looked up the literature on these lesions to see whether I could find anything that corresponded to them, and the only condition I could find was Kyrle's disease. In this case, there are hyperkeratosis of the epidermis, with penetration of the cutis, and a history of the lesions healing spontaneously, leaving excavations, the same features as those described in Kyrle's disease. Only one case has been reported in England, and only two or three in Germany, so far as I know. I saw a case resembling it in Copenhagen, in 1928.

DR. F. P. MCCARTHY: I was unable to find a case in the literature in which the observations corresponded with the pathologic picture in this case. I think that there are striking keratotic plugs in the epidermis which invaginate the corium to a decided depth. There is a slight chronic inflammatory reaction. I could not name the disease after looking over the American literature.

LUPUS ERYTHEMATOSUS OF THE FACE AND SCALP WITH DISSEMINATED LUPUS OR TOXIC DERMATITIS (GOLD). Presented by DR. BERNARD APPEL.

In C. B., a Russian housewife, aged 33, macular lesions developed on the right eyebrow three years prior to presentation. These began to enlarge twelve months before presentation, and a lesion developed over the left side of the nose. The lesions were slightly itchy. The patient was first seen at the clinic of the Boston City Hospital on May 31, 1932, and injections of gold and sodium thiosulphate were started. After the fourth injection the lesion on the nose began to get larger. After the tenth injection new lesions developed over the left upper eyelid, and in spite of treatment new lesions constantly appeared. At the end of September, 1932, a lesion about 2 inches (5 cm.) in diameter developed over the occiput. This has slowly increased in size to about 4 inches (10.1 cm.). Brownish scaly lesions have also developed over the lower part of the abdomen and both flanks in the past two months. All of the lesions are exceedingly pruritic. None has healed. The patient has typical areas of lupus erythematosus scattered over the face and scalp. The area over the occiput is irregular, sharply outlined, pink, dry and scaly, with alopecia and many punctate, keratotic, follicular plugs. The lesions over the flanks are scattered, discrete, brownish macules, two of which are slightly scaly and somewhat thickened.

The lesions have been slowly increasing in size and number. The Kahn test of the blood was negative.

DISCUSSION

DR. M. M. TOLMAN: I have seen these aurides of the French several times, resulting from the administration of gold preparations. They clear up gradually after the gold preparation is omitted. They resemble somewhat the lesions that are occasionally seen following the administration of bismuth. I suggest the administration of bismuth after the aurides clear up.

DERMATITIS ARTEFACTA SPOROTRICHOSIS (?). Presented by DR. WILLIAM J. MACDONALD.

C. S., an American, aged 36, a plumber, stated that about May 7 he was carrying some muriatic acid on his left shoulder when the vessel containing the acid broke,

and the acid trickled down his arm to the wrist. The following day another injury was sustained by the patient, namely, he received a spindle puncture on the left hypothenar eminence. This took six weeks to heal. On the following day there was slight erythema due to the muriatic acid burn, and in June, three weeks later, four lesions appeared on the forearm posteriorly, toward the ulnar side. About July 4, another lesion appeared in the middle part of the arm, followed almost immediately by a fifth, sixth and seventh over the deltoid area. At present two of the lesions are shallow, without undermining but with a distinct livid-blue margin and a slightly sanious discharge. The smaller of the two open lesions is round and coinlike, suggesting dermatitis artefacta. There was no history of the ingestion of drugs that would cause a dermatitis medicamentosa. The Wassermann reaction was negative. Biopsy was not performed as the patient was seen only once. Treatment has been surgical, some of the larger lesions having been excised.

DISCUSSION

DR. F. P. MCCARTHY: I feel that you are accepting this case on the history of the patient. I believe that no one except the patient has information other than what we have received. You have seen the patient only once. I find that he is receiving compensation. I lifted the forearm, without moving the upper part of the arm, and he complained of severe pain in the chest. I believe that the case is one of factitious dermatitis. I believe that this man produces the lesions himself.

DR. A. W. CHEEVER: A therapeutic test for syphilis should be tried. One or two of the lesions are punched out, and excoriations are frequently the starting point of syphilitic ulcerations. That fact does not account for the pain that he describes in the chest.

DR. C. G. LANE: It occurred to me that the case might be one of mixed staphylococcic and streptococcic infection, in which one organism alone is not the cause of the condition but in which a mixture of the two causes an ulcerated process that is more sluggish and slow to heal.

DR. J. H. SWARTZ: I think that the distribution rules out sporotrichosis, for abscesses do not follow the lymphatics.

DR. J. C. DOWNING: I do not agree with Dr. Lane's diagnosis, as I have had a chance to follow one of the two patients he had at the Massachusetts General Hospital, and in this man the lesions have recurred in areas previously healed. When the lesions in the shoulder were removed the scar healed without recurrence. In my opinion those areas were sealed in, and the patient did not have an opportunity to irritate them. I think that the character of the lesions presented today was not the same as those in the case I followed. In that case they were more irregular, not punched out, and had a marked red tender periphery which readily broke down. I am inclined to think that this case is a dermatitis artefacta.

SECONDARY SYPHILIS: CASE OF REINFECTION (?). Presented by DR. HENRY BENJAMIN.

An American, aged 18, a mechanic, came to the department for diseases of the skin of the Boston City Hospital on Nov. 3, 1932, with a moist dermatitis on the scrotum. A history of a penile lesion two weeks before was elicited. About a month before presentation condylomas appeared around the anus. The patient also had had a penile lesion in December, 1928. Antisyphilitic treatment was started at once and continued until January, 1931. The patient reported to the hospital every six months for blood tests, which were negative. He shows several large, moist, flat condylomas around the anus and several round and oval crusted lesions on the scrotum. The inguinal glands are enlarged. There are several small inflammatory follicular lesions on the abdomen. There are a few crusts on the scalp. There is a mucous patch on the under surface of the tongue.

There were a few positive Wassermann reactions at the beginning of the treatment in 1928. Lumbar puncture, on Nov. 22, 1930, showed a practically normal spinal fluid; white corpuscles, 2; red corpuscles, 10; total proteins, 55; Pandy test, negative; colloidal gold curve, 222210000; Kahn test, negative; Wassermann test, negative. On Nov. 3, 1932, the Wassermann reaction was positive.

DISCUSSION

DR. W. P. BOARDMAN: I object to the diagnosis of second infection. The lesions are not symmetrical. They are rather localized, and some of them are deep seated. I think that the condition resembles that in late secondary, recurring syphilis, which may occur at the end of several years, rather than early secondary syphilis, in which the eruption is generalized, symmetrical and superficial.

DERMATITIS HERPETIFORMIS (?). Presented by DR. RUDOLPH JACOBY.

M. B., a housewife, aged 55, has had an eruption on the extensor surfaces of the forearms and hands of about four months' duration. The patient states that the condition began on the back of the left hand from a "bite of a chicken," which was followed by an eruption of blisters of various sizes which itched intensely. The lesions break down, form scabs and slowly heal, and some leave scars. She has had a few itchy lesions on the neck, but no vesicles. The eruption has persisted. New lesions appear frequently. The patient has lost 15 pounds (6.8 Kg.) recently. She has been under treatment for cirrhosis of the liver for a considerable period. At presentation she showed vesicular and bullous eruptions on the extensor surfaces of both arms and hands. The bullae are on a noninflammatory base. They itch so intensely that the patient has to open them with a needle for relief. The lesions heal, with scarring. There is a dry eczematoid eruption on the neck.

The observations on the blood were consistent with secondary anemia (red cells, 3,300,000) and a chronic condition of the liver. The basal metabolism was —18. (The patient was sensitive to thyroid medication.)

The blood picture improved with liver and iron, and the cutaneous condition improved with two fractional doses of roentgen rays last October.

DISCUSSION

DR. R. JACOBY: I had to omit some of the history in this case from the record. The woman is a confirmed alcoholic, a dipsomanic. She has alcoholic cirrhosis of the liver of long duration. She first stated that the eruption came from the bite of a chicken. She also said it came from spraying plants with some kind of a spray. No Wassermann test has been made because she has refused to have it done. She has a family of healthy children and has had no miscarriages. She also has secondary anemia which can be controlled rather well by the persistent use of liver and iron. She has a low basal metabolism, —18. However, she cannot be given thyroid extract because she is sensitive to the drug. My impression is that part of the picture is factitious. That is, I believe that she does a great deal of scratching and digging; she is a very nervous person. I could not understand why those small vesicles with bullae should arise on a noninflammatory base. I do not know whether the ingestion of bad liquor plays a part in this condition. One of my impressions was that the condition might be dermatitis herpetiformis, although I have not seen a tendency toward grouping in any of the lesions.

DR. J. G. DOWNING: I think the case is one of lupus erythematosus of the Senear-Usher type.

DR. J. H. SWARTZ: I wondered whether any gastro-intestinal upsets occurred. Has she any diarrhea? I wondered whether this was not a typical late pellagra

rather than lupus. I think that the condition is fairly typical of the group of pellagra, especially with the history given by the patient.

Dr. F. P. McCarthy: I think that the diagnosis Dr. Swartz mentioned should be considered; the anemic condition may be due largely to the fact that the patient goes days without food. She eats very irregularly. Although the lesions are not symmetrical, there is a low grade dermatitis about the neck, and a diagnosis of pellagra is to be considered.

Dr. J. H. Blaisdell: I think that a diagnosis should be based on a correct interpretation of the primary lesions. The primary lesion in this case is a large vesicle and some bullae on a noninflammatory base. There are large vesicles on the forearms and small ones on the back, and the appearance of the vesicles would rule out lichen planus. My experience with pellagra has been limited, but those cases which I have seen have conformed to the three d's: dermatitis, dementia and diarrhea. In the group of dermatitis herpetiformis or pemphigus, there are groups of small vesicles and pronounced itching and, later, the resulting scar, which is typical of the pemphigus group. I think that the correct interpretation lies within that group.

Dr. A. M. Greenwood: In confirmation of Dr. Blaisdell's opinion, the lesions on the back of the hand are so characteristic that it seems to me that I should make a diagnosis of pemphigus.

Healed Secondary Lesions with Scarring Resembling Pock Marks. Presented by Dr. Walter T. Garfield.

E. S., an American housewife, aged 27, came to the Cambridge City Hospital last June with a rash which she stated began on the arms following a headache and general malaise. The lesions were described by the house officer as a fading maculopapular eruption, with some crusts and vesicles. There was no itching. A typical arsphenamine dermatitis developed after the tenth injection of neoarsphenamine. The patient stated that she had not had chickenpox.

She now shows pigmented atrophic lesions on the face which have remained after the disappearance of the rash. The Wassermann reaction was positive.

The patient has received ten injections of neoarsphenamine and five injections of bismuth.

DISCUSSION

Dr. W. T. Garfield: Dr. Smith called my attention to the fact that the lesions were rather large for chickenpox. I did not see the original lesions. They were described by the house officer in his note in the house record; he mentioned vesicular lesions. The temperature given in the house record was normal during her entire stay at the hospital.

Hidrosadenitis. Presented by Dr. Francis P. McCarthy.

F. L. K., an American woman, aged 35, has been troubled rather constantly, for many years, with recurrent small abscesses in both axillae which rupture spontaneously and, in many instances, are opened surgically. She has had an eruption also under both breasts where the lesions have been more of a papillary nature, with an occasional pustule. She has never been completely free from the condition. The patient shows considerable scarring in both axillae, with a papular, follicular eruption. There are also deep abscesses, and pus can be expressed from the follicular openings. Under both breasts there are slightly pigmented macular and papular lesions.

Biopsy of many of the sweat glands showed active hyperplasia and tremendous enlargement of the secreting cells, some glands showing cystic dilatation. There were numerous coil glands, in contrast with the hyperfunctioning cystic glands. A group of cystic glands showed atrophy of the epithelium.

For the past seven years, no results have been obtained by surgical treatment. Roentgen treatment will be given.

DISCUSSION

DR. F. P. MCCARTHY: I became interested in this case after talking with Dr. John Lane of New Haven at the recent meeting of the Atlantic Conference in Philadelphia. Dr. Lane has been making a study of hidrosadenitis, and this case conforms clinically with this diagnosis. The duration of the disease in this patient has been about eight years. She has had recurrent abscesses which have ruptured externally and subcutaneously. Such cases are frequently handled merely by surgical drainage and have been confused with a tubercular adenitis. The biopsy picture in this case is rather interesting. One slide shows an advanced suppurative process, with polymorphonuclear leukocytes and infiltration of the corium. In the other slide, which was taken from an inactive area, are shown cystic changes in the coil glands, with changes in the epithelium lining of the apocrine glands. suggesting hyperactivity. There is little literature on the pathology of this disease, and it is difficult to demonstrate the primary process within the sweat glands. Roentgen therapy is undoubtedly the best treatment in this type of case.

CLEVELAND DERMATOLOGICAL SOCIETY

J. R. DRIVER, M.D., *Secretary*

Regular Meeting, Dec. 22, 1932

E. W. NETHERTON, M.D., *Presiding*

CHRONIC PEMPHIGUS AND DIABETES. Presented by DR. H. F. DE WOLF.

A. G., a white woman, aged 68, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital, was admitted to the dermatologic service on December 8. The history, given by a son, revealed the onset of mental disturbance in 1915 and the subsequent development of a paranoid state. In 1930 the cutaneous trouble from which she now suffers developed. It has never cleared up, but has never been as severe as at present. The patient was in Windsor (Psychopathic) Hospital from Sept. 8, 1932, to the time of admittance to Cleveland City Hospital. Examination on admission to the hospital revealed pinhead to pea-sized red papules and vesicles and bullae varying in size, some being as large as pecans; these lesions involved the face, arms, buttocks, legs and, to a lesser extent, the back, thorax and abdomen. In some places the lesions were discrete; in others, confluent, especially over the axillary folds. Some of the bullae had ruptured, leaving shallow ulcers; some exuded serum, and others were covered by thin crusts. Some excoriations were present, but no residual pigmentation was seen. The mucous membrane of the mouth and throat showed several vesicles and bullae and some ruptured lesions. New vesicles and bullae continued to form on the skin, and the Nikolsky sign was present. Moderate pruritus was present. The temperature ranged from 37 to 38.8 C. (98.6 to 102 F.); the pulse rate was from 80 to 112 per minute, and the respiratory rate, from 18 to 24 per minute.

The blood count revealed: red cells, 4,750,000; white cells, 12,800; hemoglobin, 70 per cent. The differential count was: polymorphonuclears, 75 per cent, small mononuclears, 14 per cent; large mononuclears, 5 per cent; transitionals, 4 per cent, and eosinophils, 2 per cent. The Wassermann and Kline tests of the blood were negative. The urine showed albumin varying from a trace to 1 plus, and sugar varying from negative to 3 plus. The blood sugar on December 20 was 207 mg., and on December 21, 336 mg. per hundred cubic centimeters. Carbon dioxide-combining power was 43 on December 21. Urea nitrogen was 13.3 mg. per hundred cubic centimeters on December 20.

Treatment has consisted of baths of potassium permanganate and local drying applications; a diabetic diet and insulin therapy were started on December 20.

DISCUSSION

DR. J. R. DRIVER: Pemphigus, erythema multiforme and dermatitis herpetiformis will have to be considered. In favor of pemphigus are the chronicity, the characteristic lesions in the mouth and throat and the appearance of bullae from apparently normal cutaneous areas. The duration, without temporary complete remission, is against a diagnosis of erythema multiforme. The absence of residual pigmentation and the presence of only moderate itching or paresthesia would make a diagnosis of dermatitis herpetiformis unlikely. The evidence at present is in favor of pemphigus. The effect of a diabetic regimen will be followed with interest.

DR. C. L. CUMMER: I saw this patient two or three months ago when she was at Windsor Hospital. At that time she presented simply excoriations on the body. She had been under treatment for paranoia, but had been given no medication which could explain the eruption.

DR. H. N. COLE: Dr. Miskjian thinks that this condition is dermatitis herpetiformis. It is true the patient complains of pain in the skin and of pruritis, but this complaint may be related to the mental process of which Dr. Cummer speaks. This seems to be one of those borderline cases. The Vienna school believes in the identity of pemphigus and dermatitis herpetiformis. One case inclines more toward dermatitis herpetiformis and another toward pemphigus. I agree with Dr. Driver that these lesions are more characteristic of pemphigus. There is also a certain amount of prostration, which is becoming progressively worse.

DR. H. G. MISKJIAN: This eruption belongs to the group of erythematobullous diseases. Most illuminating has been the conception of transitional types of disease, brought out, if I am not mistaken, by Louis Brocq. An eruption represents the reaction of the skin to some known or unknown cause. Different skins may react differently to the same cause. While one patient may respond with an eruption classifiable as pemphigus and another with typical Duhring's disease, the cutaneous reaction of still another may take a form that will show some characters of the first disease and some of the second. My associates and I remember a case we had several years ago in City Hospital, for which Dr. Jadassohn suggested the name pemphigus pruriginosus. There is a tendency to look on chronic bullous eruptions of unknown origin as manifestations of autotoxic processes. Pemphigus is at one end of the chain and Duhring's disease at the other. In between come all the transitional disorders which partake of the characters of both diseases. The case presented is, I think, an example of this transitional type of bullous eruption; it is far closer, however, to Duhring's disease than to pemphigus. The patient has dermatitis; she has a polymorphic eruption. She states distinctly and spontaneously that she is suffering from a burning sensation over the entire skin. The lesions are, therefore, those of "dermatitis polymorphe douloureuse." The patient does not show, however, the herpetiform grouping or the pigmentation of the lesions peculiar to that disease. Those of us who have read Duhring's description of dermatitis herpetiformis, a masterpiece of descriptive dermatology, will recognize in the case shown the erythematous type of his disease. As Dr. Cole remarked, some of the erythematous patches are the result of recently healed bullae, but others are raised and infiltrated and should be considered as having developed independently of the bullae.

DR. H. F. DE WOLF: The patient is apparently diabetic. When we first saw her, her urine showed a trace of sugar. On the second examination it was negative for sugar. The blood sugar, however, was definitely pathologic. What relation this has to her cutaneous disease, I do not know. Since she was put on a diabetic diet and given insulin the blood sugar has shown considerable improvement. I hesitate to make a diagnosis in this case; the condition is not characteristic of pemphigus. The Nikolsky sign was not characteristic. Also, the lesions are pruritic. I am inclined to agree with Dr. Cole that the condition lies between Duhring's disease and pemphigus vulgaris.

DR. E. W. NETHERTON: It would be interesting to take the contents of one of the bullous lesions and make an eosinophil count. Stelwagon has done this in dermatitis herpetiformis. Whether the eosinophil count is accepted as of definite diagnostic value, I do not know. Dr. Engman several years ago found a considerable percentage of eosinophils in these cases. I feel that this condition is pemphigus.

ACUTE SYPHILITIC HEPATITIS. Presented by DR. H. F. DE WOLF.

J. H., white, aged 17, was admitted to the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital on Dec. 15, 1932. He gives a history of venereal exposure ten weeks ago. Three weeks later he noted a penile lesion which was painless and which regressed without treatment. Five weeks ago a generalized rash appeared which he states was pruritic, and two weeks later he noted that his eyes and skin were yellow. At the time of admission to the hospital he showed definite icterus of the sclerae and the skin and a generalized papulosquamous dull red eruption, with palmar and plantar papules; there were moist papules on the penis and moderate alopecia of a characteristic syphilitic type. The mucous membranes were normal. The liver was enlarged, extending 6 cm. below the costal margin, and was tender to palpation. The spleen was not palpably enlarged. There was moderate bilateral inguinal adenopathy. There has been little change in the patient's condition.

Dark-field examination of the moist papule of the penis disclosed Spirochaeta pallida. The Wassermann and Kline tests of the blood were both four plus. Examination of the spinal fluid yielded negative results. The icteric index was 37.5 on admission and has increased to 43. The urine was essentially normal except for a trace of albumin, and was negative for bile (shake test). The blood count revealed: red cells, 3,800,000; white cells, 9,600, and hemoglobin, 70 per cent.

The patient received two doses of neoarsphenamine, 0.3 and 0.45 Gm. respectively, which were followed by a sharp febrile disturbance, the temperature rising to about 38 C. (100.4 F.).

DISCUSSION

DR. H. N. COLE: Ever since I have been in practice, I have been looking for a case of acute syphilitic hepatitis. Judging from remarks in the literature, one would imagine that acute syphilitic hepatitis is not unusual. Nevertheless, although I have been in a large syphilitic clinic over twenty years, this is the first frank case which I should be willing to classify under that diagnosis. The patient had had no treatment for his syphilis, so that there could be no relation to an arsenical reaction. He then began to have symptoms of malaise and loss of weight, and almost concomitant with his secondary eruption, icterus developed. The patient was given small doses of arsphenamine; after two doses his index had risen from 37 to 43. It seems to me that in a case of this sort it would be preferable to use a preparation that is not hepatotrophic — either bismuth or mercury. Otherwise, there is a possibility that this process, instead of clearing up, may develop into acute yellow atrophy.

CHANCROID. Presented by DR. H. F. DE WOLF.

H. R., a Negro, aged 34, was admitted to the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital on Dec. 8, 1932, complaining of a destructive penile lesion of more than a year's duration. The lesion had appeared about two weeks after exposure. He said that he had not had any previous penile lesions, but that he had had a bubo in the left groin and gonorrhea many years ago. Examination gave essentially negative results except for the extensive ulcer with a dirty base and foul odor, which encircled the greater part of the coronal sulcus and produced much destruction of tissue. There was no enlargement of the inguinal lymph nodes. The Wassermann and Kline tests of the blood were

negative. Dark-field examination failed to disclose Spirochaeta pallida. The smears examined for Ducrey's bacillus and those examined for Donovan bodies did not reveal these organisms. The formol-gel test was negative. The Frei test gave positive results with two different antigens. Auto-inoculation was performed on the left upper arm on December 15. A rapidly developing ulcer soon appeared but repeated smears from it did not reveal the bacillus of Ducrey. A biopsy taken from the border of the ulcer showed only chronic inflammation.

DISCUSSION

DR. H. N. COLE: The extensive destruction and scar formation are typical of chronic chancroidal infection. I have seen several ulcers like this in the last few years that were also suspiciously like granuloma inguinale. Some of the patients were followed for several months, but Donovan's bodies were never found. The patients were treated with antimony and potassium tartrate anyway. Then suddenly Ducrey's bacilli would be found in routine examinations. The ulcers would clear up under treatment; clinically, they were chronic chancroids.

DR. H. F. DE WOLF: Unfortunately, my associates and I did not have Dmelcos antigen for use as a diagnostic help in this case. It is difficult to obtain in this country, but we hope to have a new supply soon. It is interesting to note that this patient has given a positive reaction to two different Frei antigens. There is a history of an inguinal adenitis several years ago which doubtless was produced by an attack of lymphogranuloma inguinale.

DR. J. V. VAN CLEVE: From the literature one would conclude that the European investigators have little difficulty in culturing the Ducrey bacillus. In my experience it is extremely difficult.

DR. H. G. MISKJIAN: This case is rather puzzling. The penile lesion looks like one of the chronic granulomas, especially granuloma inguinale. In all cases of chancroid in which a positive result is obtained by auto-inoculation, it is relatively easy to find Ducrey's bacillus in smears and cultures made from the pus of the ulcer. The fact that smears were negative for Ducrey's bacillus in this case leaves little room for doubt, although the most plausible diagnosis still remains that of chronic chancroid. It is noteworthy also that in a chancroid of such extensiveness there has been no involvement of inguinal glands, so far as I know.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. HENRY SHAW.

S. K., a Jewish girl, aged 19, from the service of Dr. H. N. Cole and Dr. J. R. Driver, complained of chronic diarrhea and an eruption of the face, mouth, hands and arms of five years' duration. She had had the usual diseases of childhood, and prior to the onset of her present trouble had never had any serious illness. Her father had a similar condition of the skin which had been diagnosed as lupus erythematosus, and her mother a peculiar atrophy thought to be lipodystrophy. All three persons were presented before the society by Dr. Littman (ARCH. DERMAT. & Syph. **20**:579 [Oct.] 1929). The eruption on the face, hands and arms, as stated, had started about five years previously and she had received numerous injections of gold and bismuth compounds, also roentgenotherapy locally to the lesions and various local applications, with little help. About two years ago, following an acute gastro-intestinal upset, cholecystectomy was performed. Following this persistent severe diarrhea and tenesmus developed which have continued. Stools are thin and watery, containing much mucus and no blood, and varying in number from ten to twenty-five a day. Six weeks after the cholecystectomy, appendectomy was done. During the past two years the diarrhea has been treated chiefly by enemas and colonic irrigations. A severe exacerbation of her condition followed one injection of emetine hydrochloride. During the past two years the eruption on her skin has become progressively worse, with marked involvement of the mouth. Examination revealed numerous erythematous patches

over the face, hands and forearms. The patches were symmetrically distributed and varied in size from 1 to 3 cm. in diameter. The vermilion border of the lips showed similar lesions, and the mucous membrane of the mouth contained many erythematous, denuded patches. The abdomen was slightly distended and generally tender, with a suggestion of doughy consistency. The spleen extended to within 2 inches (5 cm.) of the level of the umbilicus and was tender to palpation. The liver was 3 fingerbreadths below the costal margin. There was a nodular mass to the left of the cecum. The heart and lungs were normal.

The urine contained no albumin or sugar. The blood count revealed: red cells, 2,600,000; white cells, 5,700; hemoglobin, 45 per cent. The differential count was unimportant. The result of a benzidine test of the stool was four plus. Roentgenograms showed no evidence of organic disease of the colon. The pulmonary fields were clear.

The patient was in the hospital for about one week. Various remedies for the diarrhea decreased the stools to one a day. The temperature remained approximately normal.

DISCUSSION

DR. H. N. COLE: The case is of particular interest because of the abdominal condition. I should interpret the enlargement of the spleen and liver as being due to amyloid degeneration. The rather doughy consistency of the abdomen suggests a low grade tuberculous infection. It is unfortunate that tuberculin tests were not made, for if the patient revealed anergy, the diagnosis would be practically clinched. The relationship between abdominal and cutaneous conditions recalls the recent work of Kren in Vienna, who, by means of blood cultures, found that in cases of lupus erythematosus positive cultures of tubercle bacilli were found in almost 100 per cent of the cases in which multiple cultures were taken. This work forces one to take a somewhat different attitude toward lupus erythematosus; perhaps many patients should be treated from the point of view of systemic infection also.

DR. H. G. MISKJIAN: In thinking of the cutaneous lesions, I have been impressed by the fact that some of them are blue or violaceous. I wonder if the association of lupus vulgaris with lupus erythematosus on the face is not possible? Some of the lesions on the hands look different from those of lupus erythematosus. I am not unaware of the fact that in atlases one sees pictures like this represented as lupus erythematosus. But I think it might be worth while to investigate further. This patient has a disease affecting the liver and the spleen at the same time, without ascites, so far as I can tell. The list of all the different entities that give rise to increase in the size of the liver and the spleen is long; it begins with the different types of hypertrophic cirrhosis and includes the leukemic syndromes and many other rare diseases. The question is: Can tuberculosis gives rise to hypertrophy of the spleen and liver? Hepatic cirrhosis of tuberculous origin has been described, but the patient has no tuberculosis of the lungs or of any other organ, so far as can be discerned. It is also evident that this is not a case of generalized tuberculosis with lesions predominating in the liver and spleen. Can it represent chronic tuberculosis of the liver and spleen alone? If this should be the case, it would be difficult for me to conceive how the patient could live with a liver so seriously affected. The first thing to do is to establish the exact nature of the internal disease. After that the relation between this disease and the lupus erythematosus will have to be determined.

It was stated that, in spite of the diarrhea, direct examination did not reveal any local lesions in the large intestine. In these days of great progress in direct examination of internal organs, one becomes puzzled when lesions are not found. One is liable to forget that there are a good many diseases that produce functional disorders without local lesions. In this instance, the diarrhea may well have been a functional disturbance arising from the condition of the liver.

SECONDARY SYPHILIS (SYPHILITIC MENINGITIS). Presented by DR. H. F. DE WOLF.

R. S., a Negro, aged 25, single, was admitted to the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital on Oct. 27, 1932. He gave a history that early in June, 1932, a penile lesion developed in the region of the frenum. Three weeks later, an eruption appeared on the arms and legs. A diagnosis of secondary syphilis was made by his physician. The Wassermann test of the blood was four plus. The patient had received two injections of neoarsphenamine, 0.6 Gm. each, intravenously, and the lesions rapidly disappeared, but he failed to continue the treatment. On October 18, blurred vision, a severe, constant, throbbing headache, deafness and tinnitus aurium developed rather suddenly. Physical examination at the time of admission to the hospital revealed moderate enlargement of the superficial lymph nodes, palmar and plantar papular syphiloderm, slight contraction of the left visual field and almost total deafness. The Wassermann and Kline tests of the blood were both repeatedly four plus. The spinal fluid on October 28 showed 600 cells per cubic millimeter; the Pandy reaction was four plus; the Wassermann reaction was four plus, and the gum mastic curve, 4554321000. Routine intravenous arsenical therapy with potassium iodide by mouth was instituted, and four subsequent examinations of the spinal fluid showed a diminution of the cell count and of the globulin content, and a return of the gum mastic curve to normal, the last examination being made on December 20 with the following findings: 6 cells per cubic millimeter; the Pandy test, plus-minus; the Wassermann reaction, negative in 0.1 cc. and 4 plus in 0.5 cc. and 1 cc., and the gum mastic curve normal. The deafness had practically disappeared.

DR. H. N. COLE: I have shown this case principally because of the rare involvement of the eighth nerve in acquired syphilis and the rapid response to therapy. When the man came to me for treatment, he was almost deaf; his hearing is almost normal now.

LARGE ROUND CELL SARCOMA OF THE TONGUE. Presented by DR. HENRY SHAW.

L. D., a Negro, aged 80, from the service of Dr. H. N. Cole and Dr. J. R. Driver at Lakeside Hospital, department of dermatology, Western Reserve University, complained of an ulceration and enlargement of the tongue. One year ago a small papule appeared at the tip of the tongue and in the course of a few weeks had enlarged to the size of a split pea. It ulcerated and became very painful. During the next eight or nine months, the whole tongue enlarged progressively until talking or swallowing became difficult. There was no history of syphilitic infection. The patient had not smoked for thirty years, although prior to that he smoked a pipe. Six months prior to the onset of the present illness, all of his teeth had been extracted.

Physical examination disclosed only general arteriosclerosis and a moderate amount of chronic emphysema. The tongue was enlarged to approximately twice its normal size. The dorsum of the tongue was markedly infiltrated, and the central portion was ulcerated and beefy red. There was no leukoplakia. The Wassermann test of the blood was negative. The blood counts and a differential count were normal.

From Aug. 23 to Sept. 7, 1932, the patient received five roentgen treatments to the tongue (200 kilovolts; 15 milliamperes; 50 cm. focal skin distance; 0.5 mm. of copper and 1 mm. of aluminum filter for eight minutes each treatment). Two months after roentgen treatment was started, there was no demonstrable change in the condition of the patient, and he received antisyphilitic therapy for a therapeutic trial and regular treatments of bismuth salicylate 0.2 Gm. and potassium iodide 10 minims (0.6 cc.) three times daily at weekly intervals for seven weeks. There was no change in his condition.

Biopsy by Dr. R. A. Moore showed that the squamous epithelium on each side of the ulcerated area was of the usual thickness and manifested some hyperplasia with the formation of small epithelial projections into the underlying tissue. All these, however, were covered by basal cells. In the ulcerated regions, the epithelium was hyperplastic, and was separated into irregular masses by a large number of inflammatory cells. The entire muscular mass of the tongue in all sections showed an extensive chronic severe inflammatory reaction of the granulomatous type. Between the muscles there were large and small nodules of tissue showing a reticular-like network of endothelium and numerous mononuclear and plasma cells. Some of these nodules showed a central giant cell of the Langhans type. A diagnosis of chronic inflammatory lesion of the tongue of the granulomatous type was made.

The sections were later reviewed by Dr. Alan Graham, who furnished us with the following description: The picture was essentially the same as that seen in the former sections. In the muscle tissue immediately below the areas of ulceration there were large masses of round or polyhedral cells which could not be accepted as wholly inflammatory. Mitotic figures were rare but present. There was no interstitial substance between the cells, and the cells showed no acinar grouping. A diagnosis of large round cell sarcoma was made.

DISCUSSION

DR. J. R. DRIVER: The case was unusual. Interstitial irradiation with heavily screened radium needles of low radium content according to the technic of Regaud and Cade would, I believe, be worth trying.

LYMPHOGRANULOMA INGUINALE. Presented by DR. H. F. DE WOLF.

S. T., a white man, aged 40, married, is presented from the service of Dr. H. N. Cole and Dr. J. R. Driver at Cleveland City Hospital. On Jan. 1, 1932, he had had an extramarital exposure. On January 10, he noticed a painful swelling in the left groin. He consulted a physician, who discovered on the left side of the penis a small lesion of the coronal sulcus the size of the head of a safety match. A yellow powder was applied, and after four or five days the lesion disappeared. Hot applications were applied to the swelling in the groin, and on January 13, an incision was made. Little or no pus was found. The incision failed to heal and continued to drain a serous fluid. The patient had been under treatment at Cleveland City Hospital (outpatient department and hospital) since June 23 and had received a total of 274 cc. of 1 per cent antimony and potassium tartrate intravenously in thirty doses, in interrupted courses, without appreciable benefit. Recently he had received roentgenotherapy as advised by Fernet (Le traitement radiothérapeutique de la lymphogranulomatose inguinale subaiguë, *Bull. Soc. franç. de dermat. et syph.* **38**:585, 1931). Between November 29 and December 12 he received four treatments of thirty minutes each to the left inguinal region: 200 kilovolts, 5 milliamperes, 50 cm. focal skin distance, 0.5 mm. copper, 1 mm. aluminum and of 1 cm. bakelite filters.

Physical examination at the time of presentation revealed nothing remarkable except the pathologic findings in the left inguinal region. There was marked tanning of the skin from recent heavy roentgen treatments. Above the level of the inguinal ligament were three sinuses which were draining a slight amount of thin, purulent material. There were still considerable induration and swelling of the whole region. There was a subsiding positive Frei reaction on the flexor aspect of the left forearm (the antigen had been injected five days earlier).

The Wassermann and Kline tests of the blood had been negative on several occasions. There was a slight degree of anemia; the red count was 4,250,000. Frei tests had been positive several times with five different antigens.

CHICAGO DERMATOLOGICAL SOCIETY

E. A. OLIVER, M.D., *Secretary*

Regular Meeting, Nov. 16, 1932

MICHAEL H. EBERT, M.D., PRESIDENT, *Presiding*

LYMPHOBLASTIC ERYTHRODERMIA. Presented by Dr. OLIVER S. ORMSBY.

This man, aged 59, presents a cutaneous condition which began on the hands and wrists six months ago following severe sunburn. Redness spread from these areas over the entire cutaneous surface.

He was treated five years ago for ringworm of the feet and for a secondary dermatitis induced by local medication.

In 1929 he had a weeping dermatitis of the legs.

There has been no change in the size of the spleen, and the lymphatic glands are not enlarged.

A differential blood count on October 21 revealed: neutrophils, 48 per cent; eosinophils, 3 per cent; large mononuclears, 5 per cent; small mononuclears, 40 per cent; lymphoblasts, 3 per cent, and transitionals, 1 per cent. On October 31, the leukocytes numbered 11,950. On November 4, they numbered 12,600, and the differential count showed: neutrophils, 41 per cent; eosinophils, 8 per cent; large mononuclears, 8 per cent; small mononuclears, 42 per cent, and transitionals, 1 per cent.

On examination, the skin of the hands and wrists was a diffuse dark red. The redness on the extremities and trunk was not so highly developed. There was some thickening as well as scaling of the skin on the trunk, and the legs showed some evidence of traumatic dermatitis. Six weeks' treatment has had no effect on the color of the skin and little effect on the itching.

DISCUSSION

DR. HAMILTON MONTGOMERY: I was especially interested in the increase in the number of monocytes. My associates and I had under observation a patient whose condition at first seemed to be eczema and was so diagnosed clinically; biopsy, however, suggested early lymphoblastoma. During the three years that the patient was under observation the white blood cell counts and differential smears were essentially normal except for a slight increase in the monocytes. Clinically, the picture of granuloma fungoides gradually developed. Roentgenotherapy produced involution of the lesions. Three other biopsies showed definite evidence of lymphoblastoma. The histologic picture in some sections suggested lymphatic leukemia and in others mycosis fungoides, but for the most part it was nonspecific. The patient died about a month ago. He no longer presented lesions of mycosis fungoides. Just before death there were hemorrhagic lesions in the skin. Postmortem examination established the diagnosis of monocytic leukemia of the Schilling type. In view of the absence of change in the blood during the early part of the disease, it would seem that lymphoblastoma started primarily in the skin and later involved internal organs.

Fraser emphasized the association of mycosis fungoides with the reticuloendothelial system of the skin. Dr. Ormsby's case presents changes in the blood that are suggestive without being diagnostic, but I believe that the condition will eventuate in one of the lymphoblastomas. I think that in many cases erythrodermia may perhaps be regarded as starting in the skin and only secondarily involving other organs.

DR. OLIVER S. ORMSBY: About three years ago I presented a patient with similar erythrodermia. In that case as well as this one the color differed somewhat from that ordinarily seen in this condition. The former patient had general

adenopathy, and the blood was normal. He was treated for a year and a half or more without change in the severe pruritus or in the redness of the skin. Some time later, after exposure to the wind during a long drive in an automobile, an acute dermatitis developed on the face and spread to the body, and within a short time the blood picture changed to that of leukemia. The patient presented here shows all the manifestations, including intense itching, noted in the previous case with the exception of adenopathy. I think that intense itching is in this type of erythrodermia characteristic, and that in both cases the condition belongs to the lymphoblastoma group.

LUPUS ERYTHEMATOSUS (TELANGIECTATIC TYPE); EPITHELIOMA (BASAL CELL); HEMATOPORPHYRINURIA. Presented by DR. L. A. BRUNSTING and DR. RUBEN NOMLAND.

This girl, aged 15, was presented before the society on two previous occasions, and because of further developments she is presented again.

The eruption began at the age of 1 year, following the application of an ointment for "pimples" on the face. Red areas developed on the cheeks, nose and forehead; they have persisted in much the same condition, although there has been scaling on some occasions.

At the Mayo Clinic general and laboratory examinations revealed the following: The patient was a dwarf, 56 inches (142.2 cm.) tall and weighing 95 pounds (43.1 Kg.). The basal metabolic rate was —22. She had begun to menstruate at the age of 10, and showed moderate generalized hypertrichosis. These findings led Dr. Wilder to the conclusion that she probably had multiple endocrine dysfunction.

Hematoporphyrin was demonstrated in the urine, and there is a definite history of hypersensitiveness to light.

Within the last three months a "sore" appeared on the cheek at the left side of the nose. This is practically covered by a crust, but at intervals the crust has come off and bleeding has resulted.

On examination, this lesion was about 5 mm. in diameter, was crusted in the center and showed a fine, rolled, translucent border. The eruption was present in well demarcated red patches on both cheeks and over most of the nose; on the forehead and chin there were less distinct areas of redness. There was no scaling. Small vessels could be seen in many places, and most of the color could be expressed by glass pressure. There were several milia on the cheeks.

DISCUSSION

DR. OLIVER S. ORMSBY: I saw this patient as an infant and reported her case before the American Dermatological Association. The patient was one of the youngest persons in whom lupus erythematosus had been reported. The disease began at the age of 18 months. Some of the members thought that it might not be lupus erythematosus, but time has demonstrated the correctness of the diagnosis.

DR. HAMILTON MONTGOMERY: When this patient was at the Mayo Clinic recently the disease was in remission; hence hereditary telangiectasia of Osler was considered in differential diagnosis. Biopsy, however, revealed the typical histopathologic picture of subacute disseminated lupus erythematosus.

CONGENITAL AURICULAR FISTULA (WITH PREAURICULAR SINUS). Presented by DR. CLEVELAND J. WHITE.

A boy, aged 5, presents a discharging ulcer about ½ inch (1 cm.) anterior to the right ear, which has been present for two years. When observed several weeks ago the ulcer had intermittently discharged. In the upper part of the preauricular region on each side there was a small, crater-like depression with a central aperture. Because of the persistence of the discharging ulcer, tuberculosis was suspected at first, but further study and the opportunity to see a similar patient in Dr. Becker's clinic made possible an exact diagnosis.

The father, an older brother and an older sister of the patient have a similar depression in each preauricular area. None of them has had any trouble. The mother and another sister do not have the condition. No member of the family has any other developmental defects.

DISCUSSION

DR. OLIVER S. ORMSBY: Patients with lesions of this type probably consult surgeons. However, dermatologists see an occasional case. Less than two months ago I saw one in which operation had been performed, but recurrence had taken place. No other members of the patient's family were affected.

DR. S. W. BECKER: I agree that these patients do not come to the dermatologists, but I feel that the cases are not as infrequent as one might believe. I have seen two in the last four years, the first of which was seen by several physicians in Chicago. At biopsy a diagnosis of tuberculosis was made. The patient was sent to the dermatologic clinic for ultraviolet ray therapy, and a diagnosis of preauricular sinus was made. The second patient was seen in the pediatric clinic recently, where the diagnosis was infected cyst. The diagnosis of preauricular sinus was confirmed, and it was possible to express a drop of pus from the lesion near the ear. My associates and I also found bilateral sinus in a patient who presented lupus erythematosus. He called my attention to a lesion just beneath the nose which I had not seen before. These developmental defects are probably not infrequent, but when they become infected the patients do not consult dermatologists.

DR. CLARK W. FINNERUD: Are not these lesions analogous to thyroglossal cysts?

DR. CLEVELAND J. WHITE: Cases of preauricular fistula are diagnosed by the surgeon as a rule, but there are few reports in the literature. Schüller (*München. med. Wchnschr.* **76**:160, 1929) expressed the belief that the degree of abnormality in a certain sense seems to be inheritable. Laurence Montgomery (*S. Clin. North America* **2**:141 [Feb.] 1931) reported three cases seen in one family, in one of which symptoms of a discharging fistula were presented. The latter was probably the first case reported in this country. The symptoms depend, of course, on whether the fistulous tract becomes infected or there is a retention cyst.

In the family of my patient, the father, one brother and one sister are also affected. The lesion will be removed surgically. It is considered to be a remnant of the first branchial cleft. While an occasional sinus may lead to the middle ear, the greatest number are short fistulous tracts that cause no symptoms.

DR. MICHAEL H. EBERT: I remember a report in the German literature of a branchial arch that persisted and manifested itself in a cartilaginous nodule anterior to the ear. In the case presented here a cleft has persisted.

DR. MAX S. WIEN: About a year ago my associates and I observed a case of preauricular cyst of this type. Yesterday we saw a preauricular cyst in the chin of a girl with a low grade infection and secondary granulomatous changes that suggested cutaneous tuberculosis.

LYMPHOGRANULOMA INGUINALE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

J. W., a Negro, aged 27, was admitted to the Cook County Hospital on Nov. 11, 1932, complaining of bilateral painful swelling of the inguinal region of eight days' duration.

Examination revealed bilateral fist-sized masses in both inguinal regions, which were fluctuant in the center and indurated at the periphery. There was slight tenderness on palpation. On the dorsum of the penis was an involuting, crusted, erosive lesion, the size of a split pea, of which the patient was unaware.

A Frei test made on November 11 with antigen furnished by Dr. Cole was strongly positive in forty-eight hours.

GRANULOMA INGUINALE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

E. D., a Negro, aged 44, who has been in the Cook County Hospital since June 25, 1932, is presented in order to compare the result of the Frei test with that in the patient just shown.

This patient has had an extensive granuloma inguinale for six years, with edema of the penis for the past four years. Donovan bodies were isolated from the lesion.

A Frei test made on November 11 with the same antigen that was used in the preceding case was negative.

LYMPHOGRANULOMA INGUINALE. Presented by DR. F. E. SENEAR and DR. MAX S. WIEN.

F. B., a white man, aged 66, born in Germany, was first presented at the meeting of the society in March, 1932, and the complete history was published in the proceedings (ARCH. DERMAT. & SYPH. **26**:1104 [Dec.] 1932).

He has been given subcutaneous injections of Frei type antigen, prepared from his own pus, which gave positive results in all cases tested with another Frei antigen which was known to be positive, supplied by Dr. Cole and his co-workers. The injections were given as suggested by Hermans (*Klin. Wchnschr.* **7**:2436 [Dec.] 1928), at from four to seven day intervals, since June, 1932. There has been considerable improvement in the local condition, evidenced by cessation of activity of and drainage from the granulomatous lesions in the groin and marked puckering and contraction of the scars from the fibrosis of the healing process.

LYMPHOGRANULOMA INGUINALE. Presented by DR. F. E. SENEAR and DR. MAX S. WIEN.

L. B., a mulatto, aged 34, born in the United States, presents a discharging lesion of the right groin and the adjacent portion of the abdomen of eighteen months' duration. In 1916 he was operated on for a ruptured appendix, with complete healing in three months.

He was first seen by us on Aug. 30, 1932, when he gave a history of having strained his back while lifting a heavy object fifteen months previously. He had subsequently noted swelling in the groin, which was incised by a physician and continued to discharge, in spite of treatment, with the formation of new swollen areas in the groin and in adjacent portions of the thigh and abdomen.

Roentgenograms of the pelvis and complete genito-urinary examination showed no tuberculosis or other pathologic condition.

The blood serum showed no evidence of syphilis. The leukocyte count was 6,800. The differential count showed: polymorphonuclears, 63 per cent; large mononuclears, 8 per cent; lymphocytes, 28 per cent, and eosinophils, 1 per cent.

Examination disclosed in the right groin five puckered, adherent scars that were the residua of preexisting indolent, discharging, granulomatous ulcers. Single lesions were noted on the adjacent portion of the abdomen in the right lower quadrant and at the lower pole of the appendical scar.

A Frei test with antigen prepared from pus from the patient just presented was strongly positive. A second test two weeks later, with antigen supplied by Dr. Cole, also was strongly positive.

The patient has received subcutaneous injections of Frei type antigen, prepared from pus from the patient just presented, since September 26, at from four to seven day intervals. His condition has improved considerably, and at the present time the discharge from the lesions has practically ceased.

LYMPHOGRANULOMA INGUINALE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

G. L., a Negress, aged 32, was admitted to the Cook County Hospital on Nov. 2, 1932, complaining of pain in the rectum and a discharging sinus in the left buttock of two years' duration. She had been passing blood with the stool

for the past three months. Two years previously she had had a hemorrhoidectomy, and an abscess on the buttock was incised and drained, with no change in symptoms.

Examination revealed an irregular, puckered plaque the size of a silver quarter on the left buttock, with a draining central sinus. The affected skin was violaceous and indurated.

The Wassermann test of the blood was 3 plus. Vaginal smears were negative for gonorrhea. The Frei test, made with antigen supplied by Dr. Cole, was repeatedly positive.

LYMPHOGRANULOMA INGUINALE. Presented by DR. MAX S. WIEN and DR. MINNIE O. PERLSTEIN.

E. E., a Negress, aged 46, was admitted to the Cook County Hospital on Nov. 11, 1932. She stated that for the past five months she had had a leukorrheal discharge that remained unaffected by external and internal treatment. During the past twenty years she had had pain in the rectum, which was not alleviated by a hemorrhoidectomy performed three weeks before. Since the operation there had been blood in the stools in addition to the rectal pain.

Examination revealed bilateral, slightly painful, shotty inguinal adenitis and marked enlargement of the vulva, which had been first noted eighteen months before. There were pea-sized follicular lesions over the margin from which yellowish pus could be expressed which contained intracellular and extracellular diplococci.

The Wassermann test of the blood was negative. A Frei test made on the date of admission, with antigen furnished by Dr. Cole, was strongly positive in forty-eight hours.

DISCUSSION ON CASES OF LYMPHOGRANULOMA INGUINALE

DR. J. H. MITCHELL: How was the potassium and antimony tartrate that was given the patients prepared? Pardo-Castello insisted that sterilizing by heat destroys the therapeutic efficiency whereas filtration preserves it.

DR. MAX S. WIEN: These cases are presented as instances of lymphogranuloma inguinale. Zakon (ARCH. DERMAT. & SYPH. **26**:238 [Aug.] 1932) recently stated that lymphogranuloma inguinale is rare in women. This statement is true if one looks for the characteristic type of pathologic process in which a low grade infection in the groin takes place. In women in whom the primary infection occurs on the vulva, vulvar lymphangitis (esthiomène) occurs, such as has been shown here, which was named by Frei and Koppel ulcus vulvae chronicum elephantiasticum. In most cases, the lesion occurs in the vagina or on the cervix. The glandular drainage, then, is to the perirectal glands, and periproctitis develops, causing difficulty in defecation. The cases that we showed at the last meeting of the society demonstrated this genitorectal syndrome. In some cases, a true ulcerative proctitis develops. I wish to make a statement about the anergy. We showed a case of lymphogranuloma inguinale in which the Frei test was negative. In that case we were able by cross-testing to establish definitely the diagnosis of lymphogranuloma inguinale. The patients just presented were shown to demonstrate the specificity of the Frei test. Three of them gave a positive Frei test, demonstrating definitely that the condition is typical lymphogranuloma inguinale.

DR. MINNIE O. PERLSTEIN: The only cases of extragenital lesions reported in the literature occurred in men. One was reported in a surgeon with a primary lesion on the finger and secondary axillary involvement, and one in a man with a lesion on the tongue and secondary cervical involvement. In 1931, Bartels and Biberstein named the syndrome as it occurs in women lymphadenitis granulomatodes venerea, and Sulzberger and Wolf suggested the name lymphopathia venerea in order to avoid confusion with granuloma inguinale and other conditions of similar terminology.

DR. S. W. BECKER: My associates and I recently observed two cases in a man and his wife. Neither gave a history of a primary lesion and we could find none, but both had an identical picture in the inguinal glands on the right side. Both gave a positive Frei test. I can see why the term lymphogranuloma inguinale may not be good, but I do not like any designation containing "venerea."

A CASE FOR DIAGNOSIS. LICHEN PLANUS (BULLOUS?). Presented by DR. THEODORE CORNBLEET and DR. EARLE R. PACE.

H. S., a man, aged 24, was admitted to the Cook County Hospital on Nov. 12, 1932, with a generalized pruritic eruption. He stated that the eruption had begun about three weeks before on the left leg and had spread rapidly.

Examination revealed on the neck, trunk and extremities dusky-red to purplish-red, moderately scaly patches, varying from the size of a pea to that of a palm. They were irregular in shape, margination and coalescence and seemed to be composed of confluent lichenoid papules. When seen as satellite lesions, they were polygonal, burnished or slightly scaly, violaceous, flat-topped and occasionally umbilicated. On the buccal surface of the lower lip there were whitish, macerated papules and ruptured bullae. On the shaft of the penis were a few small, burnished papules. Many similar papules were present on the palms, particularly over the thenar eminences. On the legs and the upper portions of the arms were numerous large, irregular patches of thick, very dry and hard hyperkeratosis. On the legs and back there were scattered, denuded areas, varying from the size of a pea to that of a finger-nail, and a few unruptured bullae were present on the ankles and feet. On the wrists a few typical papules with tiny central vesicles were seen, two of which had been removed for examination of the tissue.

During the past few days pustules have developed on the chin and on the ankles. The patient is also suffering from an alveolar abscess.

Since admission, without systemic treatment, there has been marked amelioration of subjective symptoms, and the individual lesions have lost many of the characteristics which led to an initial diagnosis of bullous lichen planus.

The patient says that he has not used drugs. The laboratory studies have not been completed.

The microscopic picture seems compatible with the diagnosis of lichen planus. Dr. Caro reported the following: "There was a thin nucleated scale. The epidermis was acanthotic and in places showed fusion of the rete pegs to form micropapules. In these the granular layer was greatly thickened. There was a moderate degree of intracellular edema. The basal layer was indistinct in places.

"In the upper part of the corium was a dense infiltrate composed chiefly of lymphocytes and spindle cells, with many large dark chromatophores just beneath the epidermis. Mantles of similar infiltration extended down along the hair follicles."

DISCUSSION

DR. LESTER WIEDER: I feel that certain lesions on the forearms, especially those on the extensor surfaces, on the palms and on the upper parts of the arms are typical of lichen planus. Many of the other lesions are not so well demarcated as is usual in this disease, but the general aspect, except for the nondescript appearance of the involuting bullous lesions, is very suggestive of lichen planus.

DR. C. W. FINNERUD: There were characteristic lesions of lichen planus on the lips, particularly on the lower lip, although there were no lesions of the buccal mucous membrane.

DR. OLIVER S. ORMSBY: I have seen cases of this type, but they are not common. I think that a little later more of the usual lesions will be present. Over the shoulders and arms a number of typical papules of lichen planus could be seen. The condition is a type of lichen planus with bullae that occurs at times.

DR. M. H. EBERT: I saw this patient on admission and thought that the condition was an extraordinary form of lichen planus with the usual lesions and bullous lesions occurring on the bases of papules, and in addition palmar and plantar lesions, lesions on the lips and hypertrophic lesions on the legs. I have seen no reason to change this diagnosis.

DR. J. H. MITCHELL: Has arsenic or arsphenamine been given?

DR. M. H. EBERT: We questioned the patient carefully and could obtain no history of the ingestion of any medicine. He was poorly nourished when he entered the hospital, but since then his condition has improved, and the lichen planus also has improved spontaneously.

DR. J. H. MITCHELL: In a recent number of the *Dermatologische Zeitschrift* several cases are reported in which true lichen planus occurred following the use of arsphenamine. The eruption could be reproduced at will in one case.

DERMATITIS MEDICAMENTOSA (BISMUTH). Presented by DR. E. A. SKOLNIK (by invitation).

This patient, a white man, aged 43, was first seen at the Central Free Dispensary on July 18, 1932, with a genital chancre. Dark-field examination gave positive results. Between July 18 and September 8 he received ten injections of neoarsphenamine, the last four being combined with intramuscular injections of bismuth salicylate. Since September 8 he has been given eight more intramuscular injections of bismuth salicylate, at weekly intervals. Before the last injection he complained of a pruritic eruption.

Examination revealed on the neck and the upper part of both arms oval, pinkish-red, scaly, macular lesions resembling those of pityriasis rosea. One more injection of bismuth salicylate was given, and the patient was seen again within a week. At that time the lesions had become intensified and confluent, and a scaly dermatitis involved the neck, the arms, the lower part of the trunk and the legs.

DISCUSSION

DR. E. A. OLIVER: I am glad to see this case. At St. Luke's Hospital my associates and I have used bismuth a great deal during the past three years and have never seen a pityriasis rosea-like eruption following its administration. I do not think that this eruption resembles pityriasis rosea greatly, but it is interesting. We have recently seen two cases of beginning arsphenamine dermatitis in which for about three weeks the condition was typical of pityriasis rosea. Although there was a history of ingestion of arsenic, we did not suspect it until the picture of an arsphenamine eruption manifested itself. I think cases of the type presented here must be rather infrequent, for I have used a great deal of bismuth but have never seen an eruption of this kind in my own practice.

DR. M. H. EBERT: My associates and I had a patient in the ward with an eruption resembling somewhat pityriasis rosea and somewhat a toxic eruption. We obtained a history of the patient's receiving intramuscular injections, probably of bismuth, and roentgenograms of the gluteal region showed deposits still present. It would be interesting to see if deposits are still present in this case. I should like to know whether Dr. Skolnik thinks that such an eruption is precipitated as often by water-soluble preparations of bismuth as by suspensions in oil.

DR. C. W. FINNERUD: What bismuth preparation has been in use at the dispensary. I think that Dr. Skolnik and Dr. Axleshire have had more than twenty cases of this dermatitis.

DR. THEODORE CORNBLEET: Have patch tests been made?

DR. E. A. SKOLNIK: My associates and I have observed some reactions with sodium bismuth tartrate solution in water as well as with bismuth tartrate in oil.

We have made patch tests in several cases but have had no reaction. We have used both soluble and insoluble bismuth preparations, but so far have had no reaction.

DR. J. H. MITCHELL: Has the cutaneous test been used?

DR. E. A. SKOLNIK: No, only the patch test.

DR. EUGENE P. LIEBERTHAL: Is there any peanut oil in the preparation that was used?

DR. E. A. SKOLNIK: There is supposed to be peanut oil in the preparation, but in the cases in which we used the tartrate we have had the same reactions.

DR. S. W. BECKER: What happens to the patients if treatment is continued? I have seen several patients who showed a bizarre dermatitis, but I have never stopped the administration of bismuth entirely. I wonder whether, as with arsphenamine, if the administration is not stopped a severe dermatitis develops.

DR. E. A. SKOLNIK: We have found that in some cases we can continue the administration of bismuth without trouble, as the patients become desensitized. In other cases exfoliation results if the administration of bismuth is continued, but the condition clears up well under treatment with sodium thiosulphate.

PEMPHIGUS (SENEAR-USHER TYPE). Presented by DR. M. H. EBERT and DR. B. B. BEESON.

This patient, a Jewess, aged 47, presents a bullous and crusting eruption of six months' duration. The bullae developed first on the neck and chest and spread rapidly. There was little itching. She was under treatment at the Central Free Dispensary, where she received arsenic in various forms, which apparently did not help the condition.

When the patient was first admitted to the Cook County Hospital three months ago, the cutaneous condition was similar to that now present. Over the butterfly area of the face was a seborrheic, crusting area similar to that usually described in the Senear-Usher syndrome. A differential count showed no increase in eosinophils and 68 per cent polymorphonuclears. She had a low grade fever. For about two weeks there were a few erosions in the mouth, but aside from these no lesions of the mucous membranes were seen.

After about a month's stay in the hospital she improved sufficiently to be discharged, but she was never completely free from lesions. She returned to the hospital about a week ago, since which time her condition has become aggravated.

On examination, over the butterfly area of the face was an erythematous plaque with well defined margins which involved the lower eyelids and tended to become crusted. Smaller, discrete patches of the same type were present on the cheeks and in the scalp. The body was covered with large erosions, some of which were crusted. Several flaccid bullae filled with clear fluid and surrounded by an erythematous areola were present. Nikolsky's sign was strongly positive.

DISCUSSION

DR. C. W. FINNERUD: The change in the condition within the last few weeks is remarkable. Dr. Nomland and I saw the patient at the Central Free Dispensary several times during the summer, and at that time there was no lupus erythematosus-like involvement of the face. The condition was definitely pemphigus, as it is now.

DR. THEODORE CORNBLEET: Does Dr. Ebert consider that the condition was improved as a result of the intramuscular injections of whole blood?

DR. M. H. EBERT: At the time the patient was receiving intramuscular injections of whole blood she was also receiving quinine in large doses; so it is rather difficult to evaluate the effect. The case is interesting because we have another patient who at first had lesions on the face of the Senear-Usher type and now has marked bullous lesions on the body and the extremities and is definitely sick,

although there have been no lesions in the mouth that I remember. The patient presented here shows a similar condition, as the facial lesions resemble those of lupus erythematosus.

STREPTOCOCCIC ULCER OF THE LEG. Presented by DR. J. H. MITCHELL.

This man, aged 40, was injured on the left heel in October, 1931, while at work in the stock-yards. A blister formed which was treated with hot dressings. The original blister healed, but new lesions developed above it, and ulceration occurred. On Nov. 14, 1931, the ulcerated area was excised. All kinds of wet and dry dressings, as well as plaster casts and Unna's boot, were applied, without success.

Streptococci and staphylococci were found in culture, and mixed vaccines were given.

The patient first came under my observation on July 22, 1932. The clear serous fluid contained many short chains and phagocytosed cocci. On blood agar only a hemolytic staphylococcus (aureus) was grown, but with brain broth long chains of hemolytic streptococci were grown. Agglutination of the organisms occurred with the patient's serum in high dilution.

The patient had not been seen since Sept. 2, 1932, until two days ago.

DISCUSSION

DR. E. P. ZEISLER: Has Dr. Mitchell ruled out factitious dermatitis?

DR. HAMILTON MONTGOMERY: I think that clinically the typical undermining border that O'Leary and Brunsting described in pyodermia gangrenosa is present. In most of my cases the condition was associated with colitis, but in some it was not. I think that this case is definitely one of pyodermia gangraenosa. A factitious dermatitis can be ruled out because of the deep undermining of the borders. Biopsy should reveal streptococci or staphylococci lying deep in the tissues.

DR. M. H. EBERT: Has there been marked anemia at any time?

DR. THEODORE CORNBLEET: I have seen two similar cases in which the ulcers were much larger than those in this case. In both of those cases there were marked colitis and anemia. Local applications were used in vain, but the condition cleared up entirely when treated with bacteriophage.

DR. J. H. MITCHELL: Concerning the question by Dr. Zeisler, I considered factitious dermatitis first and then a streptococcic infection. The patient was injured at the stock-yards and has received $15 weekly in compensation. The time limit for compensation is sixty-four weeks, and that limit is almost reached. As he has six children, it seems strange that he would prefer $15 a week to his regular salary, but stranger things have happened. I began treatment with potassium permanganate baths. Within a few days an eschar developed. I stripped it entirely away and sent it to Dr. Muellenberger, who tested it carefully for phenol. There was none present. I have done everything I could to trick the man to find out whether he was producing the lesion. He has been investigated in the neighborhood and, as I mentioned, has had a cast on the leg. So far as I can determine, there is no factitious element. Various local applications have been used, such as surgical solution of chlorinated soda, gentian violet, ointments and dry dressings. Since I saw him the first of September, the lesion has definitely changed in appearance. He has lost weight, and his color is poor. When he disappeared in September, I presumed that the physician who has him in charge at the stock-yards had other plans. I wrote to the surgeon last week in order to complete my records, asking what had been done. He had not seen the patient, and he sent for him to come for further observation.

DR. HAMILTON MONTGOMERY: In these cases my associates and I have found it fundamental to treat the underlying systemic condition. Even if colitis and

anemia are not found, building up the general health is of more value than local measures. Particularly in patients with colitis we have had to treat that condition before we could influence the cutaneous lesions. As the colitis improved the lesions on the skin improved under various types of local treatment.

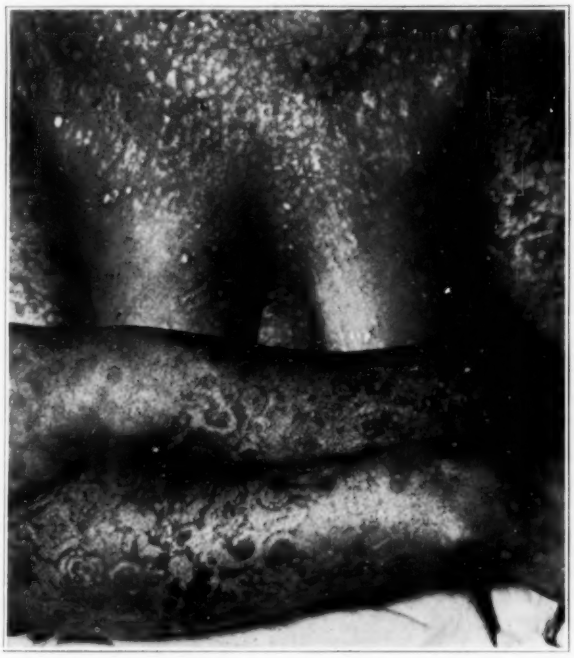
DR. J. H. MITCHELL: In the cases mentioned by Dr. Montgomery was Streptococcus enteritis found in the stools?

DR. HAMILTON MONTGOMERY: In several cases the Bargen bacillus, which is of the streptococcus group, was found.

DR. J. H. MITCHELL: In the case shown by Dr. Nomland and me about two years ago there was an active infection with Streptococcus haemolyticus. The tonsils were removed, and the man is well and carrying on his work.

A CASE FOR DIAGNOSIS (SYPHILIS?). Presented by DR. E. P. ZEISLER.

This patient, a Negress, aged 30, presents a bizarre, generalized exanthem of three weeks' duration.



Lesions in Dr. Zeisler's case.

On examination, the face, neck and trunk showed numerous discrete, pea-sized, depigmented, atrophic macules, interspersed with pale red, grouped, slightly raised follicular papules. On the arms was a curiously configurated, geographic annular macular eruption which formed a striking pattern in the skin, with here and there groups of follicular papules. The clinical picture was strikingly like that of tinea imbricata, and the depigmentation was suggestive of pinta. An indurated papule was present on the labia, and the inguinal glands were enlarged.

The Wassermann test showed: cholesterol, 1 plus, and lipoids, negative. The Kahn reaction was 2 plus.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *Secretary*

Regular Meeting, Nov. 22, 1932

GEORGE M. MACKEE, M.D., *President*

DERMATITIS ARTEFACTA. Presented by DR. GEORGE M. MACKEE.

P. de C., aged 70, a physician born in France, had been in the United States Public Health Service for twenty-six years. He had served with the French army during the World War. He stated that he had been burned on the back and sides of the neck with mustard gas, which left these areas whitish and slightly scarred. About six years prior to presentation he had a boil on the back of the neck, which was incised but which failed to heal, and an ulcer formed. The ulcer in turn was excised, but recurred larger than before. This sequence was repeated many times. The patient stated that over a period of six years, he had had twenty-two operations—many of them of the plastic type, each followed shortly afterward by recurrence. He said that, in addition, he had had roentgenotherapy treatment with ultraviolet rays and radium and many types of local applications. Superficial erosions always developed in the scarred areas with considerable rapidity, and would persist or heal again with equal speed.

The entire area, ulceration and scar tissue as well, was very tender and painful.

Specimens of the tissue taken for biopsies and at operations were variously reported as malignant and nonmalignant.

At the first examination, on Nov. 5, 1932, the patient presented a large, scarred area involving the back and sides of the neck as far anteriorly as the angles of the mandibles and extending over the posterior portion of the right shoulder and right side of the neck as far down as the midportion of the right scapula. On the back of the neck, to the right of the midline and partially within the hair line was an exudative area the size of a silver dollar; the lesion was slightly crusted about its margins. A similar eroded area with a clean granulating base and sharp, slightly raised edges, occupied a position over the upper and lateral margin of the right trapezius muscle. It was about 1 by 3 inches (2.5 by 7.6 cm.) in diameter. About the lower and lateral margins of this area were scattered discrete, pinhead-sized papular lesions, several of which were slightly crusted; according to the patient, these lesions often preceded the breaking down of the tissue. The patient admitted that he had removed pieces of tissue which he thought were preventing recovery and causing the pain. Pieces of this tissue were presented with the patient. The exudative area showed several dug-out excoriations.

Just below the scarred area, a large pedicle graft had been prepared for use if further surgical measures were to be instituted.

The case was presented as an example of extensive and severe neurotic excoriations.

HYDROA VACCINIFORME. Presented by DR. HOWARD FOX.

A. S., a boy, aged 10 years, born in the United States, of Austrian parents, had suffered from a generalized eruption since the age of 18 months. As an infant, he was fed artificially after the first week. The eruption appeared suddenly and recurred every summer with undiminished intensity. It reached its height during July and August, beginning on the first warm days of spring and continuing until cold weather. During the summer months the patient was exposed to the sun daily, but during the summer previous to presentation he was kept indoors for nineteen days, during which time the eruption improved. According to the mother's statement, the eruption always began as red spots which became blisters, the eruption being confined chiefly to the face and extremities. Itching was present for a short time after the onset of each attack.

When the patient was presented, there were no active lesions, though the physician at the New York Nursery and Child's Hospital in which the child was a patient had previously observed vesicles, pustules and crusts.

The eruption exhibited consisted of small, discrete, pitted scars with a few reddish macules scattered between them. The ears were practically free. Physical examination showed no abnormal changes in the lungs, though a roentgenogram showed an infiltration around the hilus of the right side with a definite parenchymatous lesion at the level of the third anterior interspace. A roentgenogram also showed maxillary sinusitis. Both the Mantoux test (0.02 mg.) and the control showed a reaction, but the reaction was much more intensive with old tuberculin than with the control. The Wassermann test was negative, and the urine showed nothing abnormal. Examination of the blood on two occasions showed a lymphocytosis of 58 and 88 per cent, and 12,000 and 8,100 white cells, respectively. The red cells and hemoglobin were normal. The patient was well nourished and in apparent good health.

A histologic examination made subsequent to presentation showed marked edema of the rete with formation of a large vesicle and lymphocytic infiltration in the corium. There was no evidence of tuberculosis.

DISCUSSION

DR. F. C. COMBES: I saw this child at the Willard Parker Hospital last summer, when the eruption was at its height. He then had a generalized eruption, particularly on his face, including the ears. It was quite extensive on the extremities but sparse on the trunk. Most of the lesions were flat, yellowish crusts, but there were many definite bullae. Some of the lesions were deep. There were no subjective symptoms. A history was obtained of recurrence every summer since infancy. Because of this and the extensive involvement of the face, particularly the ears, I made a diagnosis of hydroa vacciniforme, or recurring summer eruption. Although examination of the urine for hematoporphyrin was negative, this should not count against the diagnosis, as in only a relatively small number of cases is it demonstrable.

DR. HOWARD FOX: I felt somewhat hesitant about making the diagnosis, as the scars were mostly small pits, not of the type usually seen in this disease. Furthermore, the eruption affected the legs, and there were no scars on the ears. The history of recurrence every summer on exposed parts made the diagnosis seem reasonable.

PSORIASIS PUSTULOSA. Presented by DR. GEORGE M. MACKEE.

Mrs. H. F. G., aged 30, a housewife, white, said that there was no family history of similar or dissimilar cutaneous conditions, nor of asthma, hay fever, urticaria or other allergic manifestations.

The patient had had one normal child. She had had chickenpox, measles, mumps and whooping cough, but no other illnesses; she had always been active.

In July, 1931, the patient presented an eruption which began as small yellowish pustules on the volar and lateral surfaces of the palms and fingers; these soon became localized to the thenar surface of the palms. Similar lesions appeared shortly afterward on the middle of the plantar surfaces of the feet. The patient had been given the usual remedies, such as an ointment composed of 1 Gm. of salicylic acid, 2 Gm. of benzoic acid and 30 Gm. of petrolatum; iodine, chrysarobin, wet dressings, treatment with ultraviolet rays, roentgenotherapy and tar, without benefit. The condition had been constantly present since its onset, with short periods of relative improvement.

On the palms, the condition had remained confined to the thenar eminences, but on the feet the eruption had gradually spread to involve the whole of the plantar surfaces except the heels, the balls of the feet and the toes. It had extended upward to the medial and lateral surfaces of the feet to the medial surfaces of the great

toes and about the sides of the heels. Usually there was little tenderness or pain, but with exacerbations accompanied by increased erythema and infiltration, burning and tenderness were at times severe enough to interfere with walking. Frequently there was marked pruritus.

The patient had also noted a scaly area on the right frontal region of the scalp, which tended to bleed easily when the scales were removed. For four years the nail of the right index finger had been "brittle"; it repeatedly broke off close to the nail-bed. In the year before presentation all the finger-nails had become similarly affected and had appeared dry and lusterless. The general health had at no time been impaired during the course of the condition.

On examination, April 5, 1932, the lesions on the feet consisted of pustules varying in size from that of a pinpoint to that of a split pea. They remained discrete but in many places were closely aggregated on a shiny, erythematous, moderately infiltrated base. Profuse scaling in firm, thick, irregular, slightly yellowish flakes was present. The pustules were thick-walled and varied in color from yellow to greenish yellow; still others showed a central brownish discoloration. The lesions on the hands were identical in character, but the pustules were fewer, and the erythema and scaling were less marked. The eruption on the soles was sharply marginated, but on the sides of the feet and palms the boundaries were less abrupt, and the eruption faded more gradually into normal skin. From the start the lesions were definitely pustular; no vesicular lesion could be discovered.

Just within the anterior hair line there was a fairly well circumscribed area from about 1 to 1½ inches (2.5 to 4 cm.) in diameter, which showed slight erythema and infiltration and marked scaling. The scales were dry and grayish white; they could easily be removed by friction. There was a mild, fine pityriasis of the rest of the scalp.

The nails were all broken off to within from 2 to 3 mm. of the nail-bed and tended to split transversely or to separate into laminae at their margins. They were somewhat dull and moderately ridged longitudinally, but showed no pitting.

Scattered over the palms were a moderate number of pinhead to pea-sized circular areas of superficial noninflammatory, cigaret paper-like scaling characteristic of keratolysis exfoliativa. The fourth interdigital space of the feet showed slight thickening but no definite maceration or scaling.

The rest of the skin and the mucous membranes of the mouth were free from lesions.

Scales from the palms, soles, fourth interdigital spaces of the feet and roofs of the pustular lesions were negative for fungi both by extemporaneous examination and by culture at the time of the first visit, and again on May 18, 1932. Scales from the lesions of the keratolysis exfoliativa showed mosaic fungi on direct examination. Trichophytin undiluted as a patch test and diluted 1:30 as an intradermal test gave no reactions. The test was repeated on May 18. On October 4, culture from a pustule yielded Staph. albus. Culture on November 15, again yielded Staph. albus.

The Wassermann and Kahn tests were negative. Chemical examination of the blood and a blood count revealed essentially normal conditions. Repeated urinalyses revealed nothing abnormal. Biopsy on November 15, resulted in a diagnosis of psoriasis pustulosa. There was an acanthosis; the rete pegs were elongated and thinned, and the suprapapillary plates were thinned. The granular layer was absent, and there was considerable parakeratosis, the lower portion adherent, the upper part laminated. At one edge just below the horny layer, there was a large cavity, which contained red blood cells and broken up epidermic cells. About this cavity there was no spongiosis. In the center of the section, there was a similar cavity. The lower portion of the epidermis presented mild spongiosis. In the upper papillary bodies the vessels were moderately dilated, and there was a cellular infiltration composed of small, round and connective tissue cells. The papillary bodies were elongated, corresponding to the elongation of the rete pegs.

The eruption on the scalp disappeared in about three months under the nightly application of a 10 per cent ammoniated mercurial ointment.

The process on the palms and soles had advanced, apparently uninfluenced to any extent by treatment. The pustules appeared as pinpoint-sized lesions, some of which slowly increased in size and persisted for several weeks. As the lesions grew older, they tended to dry, and to darken—often to a definite brownish tone, and were gradually exfoliated in the thick scales. Frequently new pustules were present under the scales, even before they were shed. New lesions appeared almost constantly, but at times whole showers erupted almost simultaneously, together with an increase in the erythema, the infiltration and the subjective symptoms of burning and tenderness. There had been little extension of the process, and the eruption had not disappeared from any of the areas involved.

In May, an acutely erythematous, oozing, eczematous area appeared behind the right ear. This cleared within a week under wet dressings of silver nitrate in 0.25 per cent solution.

The treatment included general measures and local measures. The general measures were: (1) administration of a solution of potassium arsenite by mouth and sodium arsenate by injection; (2) for several weeks a strict diet low in protein, followed for several months by a diet relatively low in protein; (3) a diet high in vitamins, including viosterol; (4) generalized heliotherapy throughout the summer; (5) eight injections of 15 cc. each, twice weekly, of autogenous blood; (6) yellow mercurous iodide, U. S. P., at first in doses of ¼ grain (0.03 Gm.) and later of ⅛ grain (0.008 Gm.) three times daily; (7) injections of whole pituitary gland, at first ½ grain (0.03 Gm.) and later 1 grain (0.07 Gm.) three times daily; (8) injection of foreign protein in the form of autovaccine (Staph. albus), and (9) application of roentgen rays filtered with 3 mm. of aluminum to the region of the thymus according to Foerster's technic. The local measures were: (1) during the acute stages wet dressings of Burrow's solution, potassium permanganate and magnesium sulphate; (2) mercury, sulphur, sublimated bitumen, the various tars, starch, zinc oxide, salicylic acid, benzoic acid, iodine and many other drugs contained in ointments, pastes, lotions and emulsions; (3) roentgen rays, one-fourth skin unit, locally once a week for six weeks. No treatment appeared to be of benefit.

DISCUSSION

DR. J. F. FRASER: The microscopic picture suggests psoriasis. I have never seen microscopic vesicles in psoriasis. In this case there are pustular formations, the presence of which supports the diagnosis of pustular psoriasis. All the other features of psoriasis are shown in the sections. I agree with the diagnosis as presented.

DR. HOWARD FOX: I should use strong chrysarobin ointment, preferably covered with oiled silk.

DR. GEORGE M. MACKEE: Chrysarobin has been tried. Only very mild ointment is tolerated, and it has not proved efficacious. Stronger ointments cause exacerbations. That has been my experience in every case of psoriasis pustulosa.

DR. H. H. WHITEHOUSE: I should use oil of birch (crude). It has proved successful on the palms and soles—two parts of the oil to one of alcohol.

DR. GEORGE M. MACKEE: Dr. Jadassohn advised the use of yellow mercurous iodide. It was tried, without improvement.

POIKILODERMA ATROPHICANS VASCULARE. Presented by DR. FRED WISE for DR. IDA MINTZER.

Mrs. L. S., aged 31, born in this country was referred from the Jamaica Hospital to the clinic of the New York Post-Graduate Medical School and Hospital. The duration of the eruption was about seven months. The patient presented numerous stigmas of endocrine imbalance, among which were a low rate of basal metabolism, disproportionately short thighs and legs as compared with the torso and a heavy growth of coarse black hair on the lower extremities.

The eruption was most pronounced on the upper and lower extremities and on the sides of the chest, below the axillae. It consisted of a network of fine and coarse superficial capillary dilatations, some of which gave the impression of being purpuric. The color did not fade on diascopic pressure. On the anterior and posterior aspects of the shoulders the resemblance to a radiodermatitis was rather pronounced. Histologic examination confirmed the clinical diagnosis.

DISCUSSION

DR. F. C. COMBES: Several years ago, in Boston, Schwartz demonstrated bacterial occlusions in a case of poikiloderma atrophicans. I wonder if any one has ever confirmed his findings.

LUPUS ERYTHEMATOSUS PEMPHIGOIDES. Presented by DR. HOWARD FOX.

Mrs. M. A. C., aged 48, a Russian Jewess, had suffered continuously from an eruption for the two and a half years prior to presentation. It appeared first on the nostrils, next on the scalp and in the mouth and subsequently on the chest, shoulders and extremities. It was roughly symmetrical. The lesions on the trunk consisted of irregularly shaped infiltrations, varying in size from that of a split pea to that of a silver quarter. Some were smooth or slightly scaly and light reddish; others were covered with adherent brownish or blackish crusts and bled easily on slight traumatism. There were also numerous split pea-sized, coalescing, superficial, slightly depressed white scars scattered between the active lesions. On the scalp were a dozen small coin-sized, sharply defined patches which were reddish, atrophic and devoid of hair. A few were partly covered by crusts. On the occiput were numerous excoriations and blackish crusts. On the lower part of the legs were a few bluish, atrophic scars, the sites of former bullae. At the outer canthus of the right eye, arising from the palpebral conjunctiva, was a pea-sized, grayish, semisolid mass. There were also crusted lesions in the nostrils and on the ears.

The patient was of medium height and weighed 169 pounds (76.7. Kg.). She had not lost weight. Nikolsky's sign was absent, and the results of the Pels-Macht test were normal (70 per cent). The urine showed nothing abnormal. Histologic examination of a crusted lesion on the back, made by Dr. T. J. Riordan, was reported as follows: The infiltration and the pale-staining degenerated (basophilic) collagen in the upper cutis were characteristic of acute lupus erythematosus. The bullous element was not conclusive, but its location just beneath the epidermis and its appearance of having been torn away simulated pemphigus.

DISCUSSION

DR. FRED WISE: I agree with the diagnosis of disseminated lupus erythematosus with pemphigoid lesions.

LUPUS ERYTHEMATOSUS DISSEMINATUS AND PSORIASIS (?). Presented by DR. FRED WISE.

Mrs. C. W. S., aged 26, was first treated by me for lupus erythematosus disseminatus of the hands, several years previous to presentation. For two years prior to her next examination (Sept. 30, 1932), she complained of dandruff and eczema of the scalp. She was seen by several dermatologists, and the condition was variously diagnosed as psoriasis and lupus erythematosus. When she was examined in September, 1932, she presented erythematous, scaling patches on the hands and cheeks, and a scaling and erythematous eruption on the forehead, eyebrows and cheeks, with scaling of both ears and a severe scaly eruption covering the entire scalp and resembling seborrheic dermatitis, psoriasis and tinea amiantacea. On the elbows and arms there were atrophic scars, and on the chest, scattered erythematous, scale-capped papules. The finger-nails showed slight evidence of pitting, and the toe-nails definite subungual hyperkeratosis. The patient was

suffering from low blood pressure and definite secondary anemia, and had certain arthritic symptoms in the joints of the fingers and a possibility of systolic change in the heart sounds.

The Wassermann test was negative, while the result of the Kahn test was four plus.

The flexor surfaces of the fingers presented circumscribed bluish, slightly edematous lesions, with a tendency to slight scaliness in the center—mainly occupying the length of the index finger of each hand. On the upper lip there were sharply defined telangiectatic lesions.

DISCUSSION

DR. H. J. SCHWARTZ: I think the patient has both conditions.

DR. R. H. RULISON: I agree that she has the two conditions.

DR. HOWARD FOX: Though I dislike to make two diagnoses, it seems necessary in this case. The eruption on the face and scalp was typical of seborrheic eczema; that on the hands was some other condition, possibly lupus erythematosus.

DR. E. R. MALONEY: I have never seen a lupus erythematosus that looked exactly like the eruption on this woman's scalp. However, the lesions on the hands are those of lupus erythematosus, and some of the lesions on the face certainly resemble the lesions of that disease. These facts, plus the history of previous lupus lesions clearing up under treatment with gold preparations cause me to believe that we are dealing with one disease—lupus erythematosus—in all these areas.

DR. E. F. TRAUB: The lesions on the hands suggest lupus pernio rather than lupus erythematosus.

DR. HOWARD FOX: Did the patient show leukopenia? I ask this question in view of the findings of Mook in a series of cases of disseminate lupus erythematosus.

LUPUS ERYTHEMATOSUS OF THE FACE AND LICHEN PLANUS OF THE BUCCAL MUCOUS MEMBRANE. Presented by DR. BINFORD THRONE.

Anna S., a Jewess, aged 29 years, was first seen at the Stuyvesant Square Hospital on June 29, 1932. Examination at that time showed typical small plaques of lupus erythematosus on the cheeks and the nose. The patient stated that these lesions had appeared in August, 1931. The blood chemistry was normal. Examinations of the teeth and the nose and throat showed dental and tonsillar infection. These foci of infection were removed, and the sodium salt of auro-thiobenzimid-azol carboxylic acid in doses of 0.01 Gm. was given. The gold compound was not well tolerated and had to be discontinued. At this time the patient complained of some trouble in the mouth, and examination showed what appeared to be lichen planus. Biopsy showed irregular epidermis with distortion of the basal cell layer and dense infiltration in one end of the section.

On further questioning, the patient said that some years before coming to the clinic of the Skin and Cancer Hospital she had had two patches on the nose for which she had been given ten injections of a gold compound, and that the lesions in the mouth had developed after these injections.

The patient was presented as having a lupus erythematosus with lichen planus secondary to injections of a gold compound.

DISCUSSION

DR. W. J. HIGHMAN: Histologically, the lesions in the mouth looked like lichen planus.

DR. HOWARD FOX: I think that it is possible that this eruption, which has the features of lichen planus, is due to the gold compound given. I have not observed

a similar case, nor was an eruption like this a factor in any of my series of ten cases of lichen planus confined to the mouth.

DR. BINFORD THRONE: This is the second case that I have seen in which a lichenoid eruption followed the injection of a gold compound. Dr. Best showed before the Brooklyn Dermatological Society two cases of lichen spinulosus which had developed in patients with lupus erythematosus. One of these patients had been given neoarsphenamine and the other gold sodium thiosulphate, and in each case the reaction was the same—an eruption of the same type and in the same location. Both patients were women of about the same age and general physical type. These cases were reported in the Transactions of the Brooklyn Dermatological Society, in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**21**:1056 [June] 1930).

LUPUS VULGARIS TREATED WITH TRICHLORACETIC ACID. Presented by DR. R. H. RULISON.

C. M., aged 28, a handy man in a restaurant, was first seen on April 4, 1932. He had had lupus vulgaris of the front and side of the neck for twenty years. There was also a smaller patch just under the left jaw. There were marked erythema, some scaling and many apple jelly-like nodules.

The treatment had consisted in the opening up of the nodules with a pointed toothpick and the application of trichloracetic acid to the center of the tubercle with the toothpick. Treatments were given at approximately weekly intervals, the areas treated being kept rather widely separated.

The case was shown to demonstrate the cosmetic result of this treatment as compared with other methods of destruction. Several apple jelly-like nodules in the center of the diseased area remained to be treated. The reduction in erythema at the periphery of the lesion and the disappearance of the eruption under the left side of the jaw were to be noted.

VERRUCOUS TUBERCULOID PYODERMA. Presented by DR. HOWARD FOX.

P. R., aged 48, a butcher, was presented previously (March 22, 1932) as having a condition the diagnosis of which was in doubt. The patient had suffered from an extensive ulceration on the back of one hand following a wound that he had acquired while working as a butcher. Despite laboratory studies no definite diagnosis had been made. From the clinical appearance, blastomycosis and tuberculosis cutis had been considered to be the most probable diagnoses. This was also the general opinion of those who discussed the case.

Subsequent to that presentation, the patient was treated by electrodesiccation, with complete healing of the ulceration; he has remained well. The question of diagnosis was aided by an illustration in the recent textbook of Desaux and Boutilier, which simulated the lesion in this case very closely. This was the type of eruption described by Gougerot as "végétante tuberculide de la dermo-épidermite strepto-staphylococcique."

DISCUSSION

DR. FRED WISE: I compliment Dr. Fox on the excellent result which he has obtained and on the information which he has imparted with respect to the nature of the lesion.

DR. E. F. TRAUB: At the meeting of the New York Dermatological Society in February, 1930, I presented a case for diagnosis, the question being whether the localized verrucous lesion on the dorsum of the man's hand was tuberculosis or blastomycosis. The patient, completely well, together with a woman with an exactly similar lesion, but new, was shown before the same society at a subsequent time. In both these cases the same question arose, and after seeing Dr. Fox's case today I am convinced that my two cases were examples of verrucous pyoderma. This is particularly true since the only organisms that were found were a streptococcus and Staph. aureus.

MULTIPLE BENIGN CYSTIC EPITHELIOMA. Presented by DR. HANS J. SCHWARTZ.

H. M., a man, aged 35, had a marked eruption of multiple benign cystic epithelioma of the face, of gradual development over a period of seventeen years. He presented many lesions varying in size from that of a pinhead to that of a pea, especially about the lips, nasolabial fold, forehead and ears. Many of the lesions had remained discrete, but in places they had coalesced to form small, irregular, nodular tumors.

Biopsy revealed a basal cell epithelioma of the hair follicles. Many hair follicles showed evidence of malignant change, i. e., anaplasia, hyperchromatic nuclei, mitotic figures and disordered polarity.

DISCUSSION

DR. J. F. FRASER: This case belongs to the group described in the textbooks as multiple benign cystic epithelioma. In my opinion, there should be a revision of that classification. Histologically, this is a basal cell epithelioma of the hair follicles. Throughout the section one can see some normal hair follicles and others packed with anaplastic cells showing all the histologic signs of malignancy. Why not call it basal cell epithelioma? The difference is that the malignant cells in this case are confined exclusively to the follicles and are not breaking through their connective tissue lining. In basal cell cancers of the type of rodent ulcer, the malignant cells break through the so-called basement membrane and infiltrate the deep layers of the corium. This case should be classified as an intrafollicular basal cell carcinoma (carcinoma in situ).

DR. W. J. HIGHMAN: This case is a replica of one that Dr. Traub showed last spring. The question arises as to the correct nomenclature. The one form is synonymous with the huge group called syringocystoma. The other is Brooke's multiple benign cystic epithelioma, a true basal cell growth.

DR. H. J. SCHWARTZ: Has any one any suggestions to offer as to treatment?

DR. GEORGE M. MACKEE: This is a remarkable case because of the large size of the lesions and their great number, and because of the lesions in the ears. The patient is handicapped because the eruption is unsightly. In my opinion, the best way to get rid of the lesions is with surgical diathermy. A dozen or so may be removed at a time with electrodesiccation.

LOCALIZED DERMATITIS EXFOLIATIVA (ARSPHENAMINE). Presented by DR. HANS J. SCHWARTZ.

A. K., a carpenter, born in Hungary, had for twelve years been treated for psoriasis of the scalp, ears and forearms. The most recent treatment was given over a period of five weeks in March and April, 1932, and consisted of roentgenotherapy and the application of salves. He had also had chronic gonorrhea for twenty-five years, and at presentation had two urethral fistulas, chronic prostatitis, urethritis and a thick, purulent urethral discharge in which gonococci could not be found on smear or culture.

Four years prior to presentation a positive Wassermann reaction of the blood was discovered without clinical evidence of syphilis. Antisyphilitic treatment was instituted at once and twelve intravenous injections of arsphenamine were given without ill effect. The patient did not receive any more arsenic until May, 1932, when serologic examination against yielded positive results. After the third injection of arsphenamine, he noticed a small "itchy pimple" in the middle of the back. This itching area gradually increased in size over a period of eight weeks, during which time antisyphilitic treatment was given; the course consisted of eight injections of arsphenamine, four of silver arsphenamine and eighteen of bismuth; the treatment was discontinued on Oct. 7, 1932.

The patient was admitted to the department for skin diseases of the New York Hospital on Oct. 28, 1932, and was at once hospitalized. A scaling, erythematous, edematous, fissured and eczematous eruption covered the entire face, scalp, head,

neck and shoulders, and extended in a V shape over the chest and back—the apex of the V being at the level of the second costal cartilage in front and the spines of the scapulae behind. The entire back from the level of the angles of the scapulae above, to the natal cleft below was covered with a similar eruption which extended centrad a little in front of the midaxillary lines. The anterior aspect of the legs was also involved, the eruption extending symmetrically from a point just below the tibial tuberosity to the junction of the third and last fourth of the leg. The left popliteal space and adjoining parts of the left thigh and leg showed a similar eruption. The lesions on these sites had all developed during the treatment with arsphenamine and had increased slightly since its discontinuance. In the meantime, a small oval area, 4 cm. by 2 cm., had developed in the left lateral abdominal region about 8 cm. to the left of the umbilicus; this was identical with the older exfoliating lesions. The remainder of the body, including the upper extremities, the greater part of the abdomen, the thighs, the posterior aspect of the legs and the soles of the feet, was free from any eruption except the arms, which bore a few small psoriatic lesions.

On Nov. 3, 1932, patch tests were made using (*a*) 10 per cent oily suspension of bismuth salicylate; (*b*) 10 per cent neoarsphenamine in water, and (*c*) 1 per cent neoarsphenamine in water. At the end of twenty-four hours the patient complained of itching, pain and burning under patch *b*, which was removed with the others after a total application of forty-eight hours. Patches *a* and *c* were negative, but patch *b* showed from eight to ten vesicles varying in diameter from that of a pinhead to 3 mm. and an erythema which extended beyond the gauze-covered area. This patch test was markedly pruritic. Specimens of urine were examined for the presence of arsenic on October 31, November 1 and November 18. The Gutzeit test was used for the first two specimens, and the Marsh test for the last. A definitely positive result was obtained with the second specimen only, which, like the third specimen, followed an intravenous injection of 1 Gm. of sodium thiosulphate. The remainder of the examination of the urine was unimportant.

Examination of the blood showed red cells, 5,870,000; hemoglobin, 100 per cent, and white cells, 12,200; adult polymorphonuclears, 74 per cent; lymphocytes, 23 per cent; monocytes, 2 per cent, and eosinophils, 1 per cent. The blood urea nitrogen was 4 mg. per hundred cubic centimeters.

The Wassermann reaction was negative on two occasions with both cholesterolized and noncholesterolized antigens, but the results of the Kline diagnostic test with the same specimens of serum were 3 plus and 2 plus respectively.

The treatment consisted of frequent applications of a zinc oxide liniment containing 50 per cent olive oil, starch baths, forced fluids and nine daily intravenous injections of sodium thiosulphate.

The patient was discharged from the hospital on Nov. 11, 1932, considerably improved. The temperature was normal throughout, except on November 5 and 6, when it rose to 37.4 C. (99.3 F.), and the pulse maintained a rate between 80 and 90 per minute. Respiration was normal.

The psoriatic lesions on the arms were unchanged during the period of hospitalization.

This case was studied in the dermatologic wards of the New York Hospital by my associate, Dr. Arthur W. Grace to whom I am indebted for these notes.

BOWEN'S PRECANCEROUS DERMATOSIS. Presented by DR. E. F. TRAUB.

Mrs. A. R., a housewife, born in the United States, aged 50, first noticed the cutaneous condition on her right thigh and flank about ten years prior to presentation. Several small, slightly red, raised, scaly patches appeared and were treated by her physician, the end-result being a fine, thin scar. The diagnosis at the time was not known by the patient. About six to eight months prior to presentation, several more such areas appeared, all confined to the right side of the groin, thigh and flank. The lesion in the groin was the most annoying and the most

advanced. This lesion had formed a superficial ulceration and, on section, showed nothing but inflammatory tissue; a second section showed an early squamous cell epithelioma. A biopsy was performed on another lesion of quite different character just above the right buttock; a diagnosis of Bowen's disease was made clinically. This lesion did not have the classic features of the usual Bowen's disease, but histologically it seemed to fit the picture more closely.

DISCUSSION

DR. W. J. HIGHMAN: We have to conceive the condition as originally Bowen's disease, which has its distinctive attributes, gross and microscopic, the most important of which is the presence of dyskeratotic bodies in the epidermis. These are lacking in the slides I saw. There are a great many specimens, and I have not examined them all. Moreover, in some of the cases that Bowen reported, and in those of Darier, frank epithelioma was found. There is no question that this lesion is an epithelioma, and one suggesting a squamous cell growth, but I did not see the characteristics of Bowen's disease.

DR. GEORGE M. MACKEE: Some of the recent articles by Bloch and others indicate that Bowen's dermatosis may remain as such indefinitely or it may change to either squamous or basal cell epithelioma. But to make a diagnosis of Bowen's dermatosis it is necessary to have dyskeratosis, clumping of nuclei and other features of intra-epidermal carcinoma. The slides made in this case do not show these characteristics, but they do show a basal cell epithelioma. It is possible that a further histologic study will show basal cell epithelioma developing from an antecedent Bowen's dermatosis. But judging from what I see both clinically and histologically, I make the diagnosis multiple epitheliomatosis cutis—multiple basal cell epithelioma.

DR. J. F. FRASER: The most recent reference in the literature to Bowen's disease may be found in an article by Broders (Carcinoma in Situ, Contrasted with Benign Penetrating Epithelioma, *J. A. M. A.* **99**:1670 [Nov. 12] 1932). Broder classified Bowen's disease as an intra-epidermal squamous cell carcinoma. He was the first to make this classification, in a paper presented before the American Dermatological Association in 1928 (ARCH. DERMAT. & SYPH. **18**:809 [Dec.] 1928). It described the lesion as an intra-epidermal carcinoma (Carcinoma in Situ). As Bowen's disease is a histologic entity, the diagnosis in the case presented should be readily established by microscopic examination.

DR. W. J. HIGHMAN: If we are going to talk about Bowen's disease, we should confine ourselves to what Bowen described. This alone is a fair use of the man's original conception.

DR. E. F. TRAUB: It is my understanding that Dr. Barthel made the diagnosis of Bowen's disease on the third section largely for the reasons which Dr. Fraser has just stated. Dr. Jessup, who saw only the second section, had made a diagnosis of squamous cell epithelioma. The two sections presented tonight are not from the same lesion, one having been taken from an ulcerating area in the groin (the squamous cell epithelioma), and the other from a patch just above the right buttock, in which there seems to be a question of basal cell epithelioma. The latter lesion was slightly raised above the skin, and although it had a definite border, it did not have the characteristics that are usual in the average basal cell epithelioma seen on the body, since it was somewhat plaquelike and hyperkeratotic, and closely resembled Bowen's disease. Dr. Barthel felt that the lesion had none of the features of a basal cell epithelioma, because it was in the prickle cell layer. There were numerous mitotic figures in the prickle cell layer. There were marked dyskeratinization and a change in the size and shape of the prickle cells. The microscopic observations put the disease in a class of diseases caused by dyskeratinization of the prickle cell layer. The condition may develop into prickle cell epithelioma, but never into basal cell epithelioma.

GENERALIZED TUBERCULOSIS OF THE SKIN WITH SARCOID (DARIER-ROUSSY TYPE) AND MILIARY LUPUS. Presented by DR. EDWARD A. MALONEY.

F. W., a colored man, aged 25, born in the British West Indies, presented on the upper and lower extremities multiple intracutaneous and subcutaneous tumors, varying in size from that of a lentil to that of a hazelnut; some showed crusting. On the eyelids and chin were many papules varying in size from that of a pinhead to that of a lentil and resembling the papules of miliary lupus. The tumors had been present for the past ten months; the papules, for the past two months. The family history was negative, and there was no history of syphilis.

Roentgen examination of the lungs showed a moderate increase of the hilar shadow, suggesting tuberculous adenopathy. A tuberculin test was positive. The Wassermann test of the blood was negative.

Histologic examination of one of the tumors showed that the structure was that of sarcoid, of the Darier-Roussy type.

DISCUSSION

DR. H. H. WHITEHOUSE: It is an interesting and unusual case. I agree with the diagnosis.

DR. FRED WISE: I agree with the diagnosis and should be interested in discovering whether or not the patient presents in certain bones the cystic changes which sometimes accompany this type of sarcoid; a study of graduated tuberculin tests and roentgenograms of the lungs would be valuable from the diagnostic standpoint.

DR. E. R. MALONEY: A roentgen examination of the chest has been made. The roentgenograms showed apparent tuberculous involvement of the glands in the hilus of each lung. No examination of the bones has been made, but I will follow the suggestion of Dr. Wise and have that done.

IODERMA FOLLOWING THE USE OF IODINIZED TABLE SALT. Presented by DR. PAUL E. BECHET.

A. R., a man, aged 24, had had for two months an extensive papulopustular, rupial-like eruption covering the entire face and body. The lesions were innumerable and most severe. The diagnosis of syphilis was first considered, but repeated Wassermann, Kline and Kahn tests were negative. A dermatitis medicamentosa was next suspected, and the urine revealed 0.052 mg. of iodide per thousand cubic centimeters. A later test showed 100 mg. of iodide in 1,890 cc. Bromide salts were not found. The patient had been using iodized table salt in his home for a long time. Biopsy showed a fairly normal epidermis, with slight infiltration about the blood vessels, which were slightly thickened but on the whole not enlarged. The cellular infiltration was lymphocytic. There had been a marked improvement following intravenous injections of a physiologic solution of sodium chloride.

DISCUSSION

DR. P. E. BECHET: Within the past year I have had a number of patients with iododerma under observation, one of whom nearly died. All of these patients had used iodized table salt exclusively. I believe that this matter should be taken up by the local boards of health. People should be warned that the long-continued use of iodized table salt may cause a severe iododerma, which may occasionally end in death.

LYMPHOGRANULOMATOSIS CUTIS WITH LESIONS STRONGLY SUGGESTIVE OF LICHEN NITIDUS. Presented by DR. PAUL E. BECHET.

S. D., a man, aged 25, for about five years previous to presentation had had generalized adenopathy with pruritus, and his general health had been greatly affected. Several glands had been excised, and a diagnosis of Hodgkin's disease

had been made. He had received a number of treatments with high voltage roentgen rays. When he was first seen, the glands had entirely subsided as the result of the roentgenotherapy. His general health was still very poor, and he still had some pruritus. The only discernible lesions on the skin were extremely small, glistening, slightly raised, noninflammatory papules on the backs of the hands, the neck and the penis. On the neck they aggregated in patches. A roentgenogram of the chest did not disclose tuberculosis.

Examination of the blood showed: hemoglobin, 55 per cent; red cells, 2,380,000, and white cells, 8,800. The differential count was: polymorphonuclears, 91 per cent; lymphocytes, 8 per cent; mononuclears, none; basophils, 1 per cent; eosinophils, none. Examination of the urine revealed nothing significant.

The histopathologic report was that the epidermis was fairly normal, except where the rete pegs were obliterated owing to the pressure of a rather dense infiltration of round cells sharply localized in the upper corium. In these areas the basal cell layer was distorted, and the prickle cells were swollen. There was a marked amount of pigment in the upper corium and in the basal cell layer. A cellular exudate consisted of lymphocytes and some chromatophores. There was no suggestion of endothelial cells.

DISCUSSION

DR. FRED WISE: The lesions on the wrists resemble lichen nitidus, and the coexistence of Hodgkin's disease indicates that the systemic and cutaneous manifestations are dependent on the same etiologic factors.

DR. F. C. COMBES: I agree with Dr. Wise. Clinically, these papules look more like lichen nitidus than lichen planus. The only objection that I can see to such a diagnosis is that the papules do not seem shiny enough.

DR. P. E. BECHET: Dr. Wise expressed my view of the case. I thought that the condition was typical lichen nitidus and true Hodgkin's disease. I believe that the two conditions in this particular patient are due to the same etiologic factor. In view of the clinical symptoms, the report on the biopsy should be disregarded. Certainly the lesions are not those of lichen planus.

DR. J. F. FRASER: I should like to elaborate on what Dr. Wise has said. The histologic report as read does not suggest lichen planus. If the condition were lichen nitidus, the microscopic picture would establish the diagnosis. L'Esperance's recent work on Hodgkin's disease lends strong support to the view that the causative agent in that disease is the avian tubercle bacillus. The gross appearance of the cutaneous lesions is strongly suggestive of lichen nitidus. If the sections show an epithelioid reaction, inoculation of chickens with the material taken for biopsy should be performed.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. Frederick Burgess, President, Drummond Medical Bldg., Montreal.
B. Usher, Secretary-Treasurer, Medical Arts Bldg., Sherbrooke St., W., Montreal.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis Eugene Senear, Chairman, 55 E. Washington St., Chicago.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee. Time: June 12-16, 1933.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.
Place: Chicago. Time: June 8-10, 1933.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.
Place: Pittsburgh. Time: 1933.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 201 West Second St., Davenport, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November, 1933.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Frank Wilson, Secretary, 310 Greenleaf & Crosby Bldg., Jacksonville, Fla.
Place: Jacksonville, Tampa, Miami and place of meeting of state medical society.
Time: Quarterly.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Herbert H. Baukus, Secretary, 925 Delaware Ave., Buffalo.

Medical Society of the State of Pennsylvania Section on Dermatology

Stanley Crawford, President, 200, 9th St., Pittsburgh.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

G. H. Belote, Chairman, 201 S. Main St., Ann Arbor.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Grand Rapids. Time: Sept. 12-14, 1933.

Minnesota Dermatological Society

E. Z. Shapiro, President, 14 W. Superior St., Duluth.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

William E. Eastland, President, 117 N. Broadway, Oklahoma City.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

Texas Dermatological Society

T. J. Calhoun, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

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